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Clinical Predictors of Driving Simulator Performance in Drivers with Multiple Sclerosis

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Abstract

Drivers with Multiple Sclerosis (MS) experience visual-cognitive impairment that may impact their fitness to drive. Fitness to drive is the ability to control a motor vehicle, as determined via a comprehensive driving evaluation, with in-clinic and on-road driving assessments. However, the on-road driving assessment may pose a crash risk to medically at-risk drivers. Instead, a driving simulator assessment that targets the driving performance deficits of drivers may inform fitness to drive decisions. However, utilizing clinical tests to indicate driving simulator performance in drivers with MS is not fully understood.

Through three aims, this dissertation will examine the clinical utility of visual-cognitive tests to indicate driving simulator performance in drivers with MS. Aim 1 will examine the study's feasibility via evaluating recruitment capability, sample characteristics, data collection procedures, outcome measures, participants' acceptability and suitability of the driving simulator, resources to implement the study, and preliminary test results. Aim 2 will quantify if visual-cognitive tests can predict driving simulator performance in drivers with MS, when compared to control drivers without MS. Aim 3 will examine if adjustment to stimuli errors can predict the occurrence of rear-end collisions on a driving simulator.

Aim 1 findings provided the foundation for determining clinical predictions of driving simulator performance, but also identified challenges such as lower than proposed recruitment rates, missing data on the driving simulator, participants' varied responses toward the driving simulator's acceptability, and the onset of simulator sickness. Aim 2 findings showed that deficits in immediate verbal/auditory recall and divided attention can indicate driving performance deficits in drivers with MS. Aim 3 findings showed that adjustment to stimuli errors, in urban environments, and that require intermittent problem-solving and decision-making to respond and avoid collisions, may underlie driving performance deficits.

This dissertation supports the notion that it would be feasible to utilize clinical tests to indicate driving performance deficits in drivers with MS. Tests of immediate verbal/auditory recall and divided attention may be useful screening tools. Adjustment to stimuli errors in urban environments may underlie driving performance deficits in drivers with MS and can be detected on a driving simulator.

Keywords

Multiple Sclerosis, Automobile Driving, Visual Impairment, Cognitive Impairment, Computer Simulation, Driving Performance

Summary for Lay Audience

Drivers with Multiple Sclerosis (MS) experience visual-cognitive impairment (e.g., blurry or double vision, difficulty with thinking, remembering, reacting) that may impact their on-road driving performance. However, assessing on-road driving performance may pose a crash risk to medically at-risk drivers. Instead, a computer-based driving simulator assessment with realistic driving scenarios, and that target the driving performance deficits of drivers, may be useful for making decisions about one's driving performance. However, using clinical tests to indicate driving simulator performance in drivers with MS is not fully understood.

Through three aims, this dissertation will examine if using visual-cognitive clinical tests can indicate driving simulator performance in drivers with MS. Aim 1 will examine the study's advantages and disadvantages via evaluating participant recruitment strategies and characteristics, data collection procedures, outcome measures, participants' acceptability and suitability of the driving simulator, resources to implement the study, and preliminary test results. Aim 2 will examine if visual-cognitive clinical tests can detect driving simulator performance in drivers with MS, when compared to drivers without MS. Aim 3 will examine if simulated driving errors can detect those who may experience a rear-end collision on the driving simulator.

Aim 1 findings provided the foundation for determining clinical tests that can identify driving simulator performance, but also identified challenges such as lower than proposed recruitment rates, missing data on the driving simulator, participants' varied responses toward the driving simulator's acceptability, and participants experiencing discomfort on the driving simulator. Aim 2 findings showed that difficulty with remembering verbal information and divided attention can detect driving performance deficits in drivers with MS. Aim 3 findings showed that driving errors that require thinking and making decisions to respond and avoid collisions may underlie driving performance deficits in drivers with MS.

This dissertation supports the notion that it would be feasible to use clinical tests to indicate driving performance deficits in drivers with MS. Tests of verbal memory and divided attention may identify driving performance deficits. Driving errors that require thinking and making

decisions to respond and avoid collisions may underlie driving performance deficits and can be detected on a driving simulator.

Co-Authorship Statement

Chapters 1 to 4 will be submitted to journals for publication.

Sarah Krasniuk MSc, candidate for PhD in the Health and Rehabilitation Sciences at the University of Western Ontario

As the research student, Ms. Krasniuk co-conceptualized the study, completed daily administrative tasks, participant recruitment, screening, informed consent, testing procedures, data management and analysis, interpretation, manuscript writing, and research dissemination. She consulted with Dr. Miriam Monahan on the implications of study findings in Chapters 2 to 4; Dr. Sivaramakrishnam Srinivasan about a feasible and accurate method for computing and interpreting the driving simulator data for Chapter 2; Dr. Wenqing He about statistical analyses for Chapters 2 to 4; and the DriveSafety™ team about verifying driving simulator data for Chapter 2. Ms. Krasniuk will be the first and corresponding author for publications of Chapters 1 to 4 of this dissertation.

Sherrilene Classen PhD, MPH, OTR/L, FAOTA, FGSA

As the research student's supervisor and co-principal investigator of the dissertation, Dr. Classen oversaw all aspects of the study from conception to dissemination, and will be a co-author on publications for Chapters 1 to 4.

Sarah A. Morrow MD, MS, FRCPC

As the research student's co-supervisor and principal investigator of the dissertation, Dr. Morrow oversaw all aspects of the study from conception to dissemination, and will be a co-author on publications for Chapters 1 to 4.

Liliana Alvarez J. PhD, MSc., BSc (OT)

As one of the research student's advisors and co-investigator of the dissertation, Dr. Alvarez provided testing and infrastructure support in the University of Western Ontario's i-Mobile Driving Research Lab, and will be a co-author on one of the publications.

Heather Rosehart BScH

As the research coordinator of the dissertation, Ms. Rosehart completed daily administrative tasks, and assisted the research student with participant recruitment, screening, and informed consent procedures. Ms. Rosehart will be a co-author on one of the publications.

Miriam Monahan OTD, MS OTR/L, CDRS, CDI

As an occupational therapist and certified driver rehabilitation specialist consultant, Dr. Monahan contributed to the implications of study findings in Chapters 2 to 5 of the dissertation, and will be a co-author on one of the publications.

Sivaramakrishnam Srinivasan PhD

As a civil and coastal transportation research engineer consultant, Dr. Srinivasan contributed to establishing a feasible and accurate method for computing and interpreting the driving simulator data, and will be a co-author on one of the publications.

Wenqing He PhD

As a biostatistician consultant, Dr. He contributed to the research design, methods, and statistical analyses of the dissertation, and will be a co-author on one of the publications.

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List of Abbreviations

The following list includes abbreviated terminology used throughout the dissertation.

BVMTR	Brief Visuospatial Memory Test-Revised Version
CVLT2	California Verbal Learning Test-Second Edition
CDE	Comprehensive Driving Evaluation
DR	Delayed Recall
EDSS	Expanded Disability Status Scale
IR	Immediate Recall
MS	Multiple Sclerosis
PUEoU	Perceived Usefulness and Ease of Use Questionnaire
SAS	Simulator Adaptation Syndrome
SDMT	Symbol Digit Modalities Test-Oral Version
SUS	System Usability Scale
UFOV	Useful Field of View™
UFOV1	Useful Field of View™ Subtest 1, Central Visual Processing Speed
UFOV2	Useful Field of View™ Subtest 2, Divided Attention and Processing Speed
UFOV3	Useful Field of View™ Subtest 3, Selective Attention and Processing Speed

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Chapter 1

1 Literature Review

1.1 Introduction

Multiple Sclerosis (MS) is the most prevalent demyelinating disease of the central nervous system (Multiple Sclerosis International Federation, 2013; World Health Organization, 2017). The disease may lead to impairment in visual (e.g., decreased visual acuity), cognitive (e.g., slowed information processing speed), sensory (e.g., decreased proprioception), and motor ability (e.g., muscular weakness) that compromises an individual's fitness to drive (Krasniuk, Classen, Morrow, et al., 2019). Fitness to drive is the ability to control a motor vehicle on all public roads, without an increased crash risk (Brouwer & Ponds, 1994; Transportation Research Board, 2016, p. 10). An individual's fitness to drive is determined through a comprehensive driving evaluation (CDE), which includes an in-clinic and on-road driving assessment (Classen et al., 2012, p. 321-344; Classen & Lanford, 2012, p. 221-277; Di Stefano & Macdonald, 2012). However, the CDE may not be feasible for some medically at-risk drivers, as it may be expensive, not readily available, and may pose a crash risk during the on-road assessment, which occurs in real-world traffic conditions (Weaver & Bédard, 2012; Zou & Vu, 2019). Instead, a driving simulator that can measure the driving performance impairments of medically at-risk populations may feasibly inform decisions about one's fitness to drive (Allen et al., 2010; Campos et al., 2017).

Based on the extant literature, visual and cognitive impairment may impact driving performance in drivers with MS. However, little congruency exists for which visual and cognitive clinical tests predict on-road and driving simulator outcomes (Krasniuk, Classen, Morrow, et al., 2019). Notably, deficits in visual acuity, complex attention (e.g., divided, sustained), executive function (e.g., reasoning), information processing speed, visuospatial ability, and working memory indicate decreased on-road outcomes (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Classen et al., 2018; Devos et al., 2017; Krasniuk, Classen, Monahan, et al., 2019; Krasniuk, Classen, Morrow, et al., 2019; Lincoln & Radford, 2008; Morrow et al., 2018; Ranchet et al., 2015; Schultheis et al., 2010). Conversely, impairment in auditory information processing speed, divided attention, and working memory detect deficits in driving simulator outcomes (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003). These inconsistent findings make it difficult to understand if driving simulator assessments validly measure driving performance impairments in drivers with MS. Invalid decisions for unfit drivers may increase their crash risk (Archer et al., 2014). Conversely, invalid decisions for drivers who are fit to drive may lead to premature driving cessation, which may be detrimental for their independence, community mobility, or societal participation (Archer et al., 2014). To make valid fitness to drive decisions, driving simulator assessments must target real-world driving performance impairments of the medically at-risk population (Allen et al., 2010; Campos et al., 2017). Therefore, this dissertation will examine the clinical predictors of driving simulator performance using evidence-informed clinical predictors of on-road driving performance in drivers with MS. The literature review provides an overview of MS in Canada; the visual, cognitive, sensory, and motor impairments of individuals with MS that may affect driving ability; the process of determining fitness to drive in Canada; using driving simulators to assess driving performance; and the evidence on the clinical tests that predict on-road and driving simulator outcomes.

1.2 Multiple Sclerosis

Multiple Sclerosis is one of the most common neurological diseases in young to middle aged adults, with an onset between 20 and 50 years (Bishop & Rumrill, 2015; Dobson & Giovannoni, 2019). Worldwide, approximately 2.5 million individuals have MS (Multiple Sclerosis International Federation, 2016; Wallin et al., 2019). Canada has one of the highest prevalence rates at 290 per 100,000 population (Amankwah et al., 2017; Public Health Agency of Canada, 2018). Multiple Sclerosis is a chronic inflammatory disease that leads to damage to the myelin sheath of nerve fibers in the brain, spinal cord, and optic nerves (Lublin et al., 2014; Thompson, Banwell, et al., 2018; Thompson, Baranzini, et al., 2018). Lesions, or sclerotic plaques, develop due to the damaged myelin, which slow down the flow of nerve impulses and disrupt communication within the central nervous system (Lublin et al., 2014; Thompson, Banwell, et al., 2018; Thompson, Baranzini, et al., 2018). The disruption may impair visual, cognitive, sensory, and motor abilities that are essential for daily activities like driving (Fragoso et al., 2016; Krasniuk, Classen, Morrow, et al., 2019).

1.2.1 Types of Multiple Sclerosis

Individuals may have a relapsing-remitting or progressive diagnosis (Lublin et al., 2014; Thompson, Banwell, et al., 2018). About 85% of individuals have relapsing-remitting MS, which presents with episodes of inflammatory attacks that lead to new or increasing neurological dysfunction, followed by episodes of partial or complete neurological function (Lublin et al., 2014; Thompson, Banwell, et al., 2018). The onset of relapsing-remitting MS occurs between 20 and 40 years, affects women two to three times more than men, and typically presents with more brain lesions, which may lead to sensory or cognitive impairment (Lublin et al., 2014; Thompson, Banwell, et al., 2018).

Conversely, about 15% of individuals have progressive MS, which presents with a progressive accumulation of neurological impairment over time from disease onset (i.e., primary progressive) or following a relapsing-remitting disease course (i.e., secondary progressive; Lublin et al., 2014; Thompson, Banwell, et al., 2018). The onset of progressive MS occurs between 40 and 60 years, affects women and men equally, and typically presents with more spinal cord lesions, which may lead to motor impairment (Lublin et al., 2014; Thompson, Banwell, et al., 2018). Nevertheless, individuals with relapsing-remitting MS or progressive MS can experience variable intensities or combinations of visual, cognitive, sensory, or motor impairment that may negatively affect their driving ability (De Sonneville et al., 2002; Huijbregts et al., 2004).

1.2.2 Visual Impairment

Visual impairment is prevalent in up to 90% of individuals with MS (Graves & Balcer, 2010; Nerrant & Tilikete, 2017). Visual disorders associated with MS, including optic neuritis or ocular motor dysfunctions (e.g., nystagmus, internuclear ophthalmoplegia) may lead to mild to progressive impairment in colour perception, contrast sensitivity, depth perception, glare recovery, peripheral field of view, and/or visual acuity (Graves &

Balcer, 2010; Nerrant & Tilikete, 2017). Such visual impairment may affect the ability to detect and react to roadway information (Classen et al., 2018; Devos et al., 2017; Krasniuk, Classen, Morrow, et al., 2019).

1.2.3 Cognitive Impairment

Cognitive impairment is prevalent in up to 75% of individuals with MS (Bobholz & Rao, 2003; Korakas & Tsolaki, 2016). Individuals may experience decreases in complex attention (e.g., divided attention), episodic memory and learning (e.g., verbal, visuospatial), executive function (e.g., reasoning), expressive language (e.g., verbal fluency), information processing speed, visuospatial ability, and/or working memory (Bobholz & Rao, 2003; Korakas & Tsolaki, 2016). Such cognitive impairment may impact the ability to process, attend, prioritize, respond, think, or make decisions when driving (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Devos et al., 2017; Krasniuk, Classen, Morrow, et al., 2019; Lincoln & Radford, 2008; Morrow et al., 2018; Schultheis et al., 2010).

1.2.4 Sensory Impairment

Sensory impairment is prevalent in up to 90% of individuals with MS (Scherder et al., 2018; Svendsen et al., 2005; Uszynski et al., 2016). Individuals may experience paresthesia (e.g., prickling sensation, tingling, painful burning), hypesthesia (e.g., reduced sensation, numbness), neuropathic pain, and losses in proprioception, which may impact their physical ability to operate a motor vehicle (Scherder et al., 2018; Svendsen et al., 2005; Uszynski et al., 2016).

1.2.5 Motor Impairment

Motor impairment is prevalent in up to 90% of individuals with MS (Fielding & Clough, 2019, p. 163-185). Individuals may experience losses in coordination, control, and/or muscular strength, which may impact their physical ability to operate a motor vehicle (Marcotte et al., 2008; Schultheis et al., 2009).

1.3 The Process of Determining Fitness to Drive in Canada

As individuals with MS can experience varying intensities of visual, cognitive, sensory, and/or motor impairment, assessing driving abilities is necessary and essential for determining fitness to drive. Fitness to drive is the ability to operate, control, and maneuver a motor vehicle, with or without technology, on all public roads (Brouwer & Ponds, 1994; Transportation Research Board, 2016, p. 10). As driving is a privilege and not a right, an individual's fitness to drive is based on the ability to follow the road safety rules and traffic laws of the jurisdiction, without compromising the health and safety (i.e., crash risk) of other road users (i.e., pedestrians, cyclists, vehicles; Canadian Council of Motor Transport Administrators, 2020, p. 8-11; Canadian Medical Association, 2019, p. 11-15). Accordingly, fitness to drive has legal implications, and to drive legally, individuals must meet the jurisdiction's standards for driving (Canadian Council of Motor Transport Administrators, 2020, p. 8-11; Canadian Medical Association, 2019, p. 11-15).

In Canada, an individual's fitness to drive is determined through a risk management approach (Canadian Council of Motor Transport Administrators, 2020, p. 8-11). The approach ensures that fitness to drive determinations are not solely based on medical conditions, diagnoses, or presumed group characteristics. Rather, the approach considers the best available evidence, via a CDE that includes an in-clinic and real-world driving assessment (Canadian Council of Motor Transport Administrators, 2020, p. 8-11).

1.3.1 Identifying At-risk Drivers

Often, physicians are the first to identify at-risk drivers—those who may be unfit to drive (Canadian Medical Association, 2019, p. 3). Additionally, at-risk drivers may be identified via themselves, their caregivers or loved ones, or other healthcare professionals (Vrkljan et al., 2013). In Canada, physicians and other healthcare professionals, such as nurse practitioners, optometrists, and occupational therapists, have a mandatory or discretionary responsibility to report medically at-risk drivers to their province's Ministry or Department of Transportation (Canadian Council of Motor Transport Administrators, 2020, p. 8; Canadian Medical Association, 2019, p. 8-11). Upon receiving medical reports from these healthcare professionals, the Ministry of Transportation may refer at-risk drivers to complete a CDE to determine fitness to drive, administered by an occupational therapist and a licensed driving school instructor (Canadian Council of Motor Transport Administrators, 2020, p. 17; Canadian Medical Association, 2019, p. 8-10).

1.3.2 Assessing Fitness to Drive

1.3.2.1 In-Clinic Assessment

The in-clinic assessment may include a review of medical and/or driving history, and a clinical assessment of visual, cognitive, sensory, and motor abilities (Canadian Council of Motor Transport Administrators, 2020, p. 32-40). Though typically administered by occupational therapists, other healthcare professionals such as general or specialized physicians, nurse practitioners, physiotherapists, rehabilitation assistants, or community support workers may be involved in the assessment process (Vrkljan et al., 2013).

1.3.2.1.1 Review of Medical History

A review of medical history, via an individual’s medical charts, test results, reports, or diagnostic images, may provide information about the driver’s health, medical condition(s), compliance with and/or response to treatment (Canadian Council of Motor Transport Administrators, 2020, p. 34). Such information may help determine whether the individuals’ health or medical condition(s) are new, stable, or progressing, and whether their conditions may impact fitness to drive.

1.3.2.1.2 Review of Driving History

The review of driving history via an individual’s driving record may provide previous and current information about one’s driving status (e.g., valid, cancelled, suspended), exposure (e.g., years of having license), or conditions (e.g., vision requirements). Other information may indicate whether the driver has any driving offences, sanctions, or motor vehicle related Canadian Criminal Code convictions, crash history, or past road test results (Ministry of Transportation of Ontario, 2018). This information may provide insight to whether the driver may experience losses in driving abilities or behaviours that may increase crash risk or affect fitness to drive, and whether this information has been previously documented.

1.3.2.1.3 Clinical Assessment

The clinical assessment examines if drivers experience impairment in visual, cognitive, sensory, and/or motor abilities needed for driving (Canadian Council of Motor Transport Administrators, 2020, p. 32-40). Understanding if drivers experience such impairments may inform whether they may have difficulty operating, controlling, and maneuvering a vehicle in various traffic and environmental conditions prior to undergoing the on-road assessment (Transportation Research Board, 2016, p. 9).

1.3.2.2 On-Road Assessment

1.3.2.2.1 Environment

The on-road assessment is administered by an occupational therapist and a licensed driving school instructor (Canadian Council of Motor Transport Administrators, 2020, p. 8-10). The assessment informs fitness to drive decisions via the driver's ability to operate, control, and maneuver a vehicle while detecting, judging, and responding to roadway information in residential, suburban, urban and highway environments (Classen et al., 2017; Justiss et al., 2006).

1.3.2.2.2 Driving Maneuvers

During the on-road assessment, the licensed driving school instructor, who sits beside the driver and provides navigational instruction, ensures overall vehicle safety, which may include verbal and/or physical intervention (Fox et al., 1998). The occupational therapist, who sits behind the passenger seat, assesses the driver's operational and tactical maneuvers (not often strategic driving maneuvers) when driving straight, reversing, stopping, yielding, crossing through intersections, making left or right turns or lane changes, overtaking other vehicles, or merging (Justiss et al., 2006; Korner-Bitensky et al., 2005; Michon, 1985; Odenheimer et al., 1994).

Operational driving maneuvers occur within seconds and require automatic and habitual visual and motor abilities to search, scan, recognize, prioritize, react, and respond to information in the driving environment (Michon, 1985; Transportation Research Board, 2016, p. 8). Such maneuvers may involve physically operating the vehicle controls, such as pressing the accelerator or brake pedals to respond to environmental stimuli like traffic signs or other road users (Michon, 1985; Transportation Research Board, 2016, p. 8).

Tactical driving maneuvers occur within seconds to minutes and require cognitive abilities to intermittently problem-solve and make decisions when maneuvering in an environment (Michon, 1985; Transportation Research Board, 2016, p. 8). Such maneuvers may involve judging the space and time required when crossing in front of or across oncoming traffic (Michon, 1985; Transportation Research Board, 2016, p. 8).

Strategic driving maneuvers can occur within minutes (for an on-road assessment) and require higher-order cognitive ability, including attention, visual-perception, memory, and executive function (e.g., reasoning, insight) to assess, initiate, plan, reason, decide, and problem solve driving in the environment (Barco et al., 2012; Michon, 1985; Transportation Research Board, 2016, p. 8). Such maneuvers may consider the rules, laws, and flow of traffic, and the risks and challenges of driving tasks, traffic and environmental conditions (Michon, 1985; Transportation Research Board, 2016, p. 8). Further, strategic driving maneuvers may involve the long-term or short-term preparations of navigating a route beforehand or adapting to changes when navigating a route in real-time (Barco et al., 2012; Michon, 1985; Transportation Research Board, 2016, p. 8). As driving assessors typically provide instructions throughout the road course, strategic driving maneuvers are not often assessed. However, such maneuvers may be assessed if the on-road assessment incorporates a task that requires drivers to independently problem solve or navigate, such as determine the best route among numerous options to exit a busy parking lot (Barco et al., 2012; Krasniuk, Classen, Monahan, et al., 2019; Michon, 1985).

1.3.2.2.3 Outcomes

Driving outcomes may include a global rating score, such as pass vs. fail, which is based on the judgment of the occupational therapist and licensed driving school instructor (Justiss et al., 2006; Korner-Bitensky et al., 2005; Odenheimer et al., 1994). Other driving outcomes may include the number and/or severity of driving errors when maneuvering through the road course (Justiss et al., 2006; Korner-Bitensky et al., 2005; Odenheimer et al., 1994). In the literature, studies document driving errors in: *adjustment to stimuli* (operational or tactical maneuver), responding to critical roadway information while disregarding redundant information; *gap acceptance* (tactical maneuver), judging an appropriate safe time or distance to cross in front of or when approaching traffic; *lane maintenance* (operational or tactical maneuver), steering the vehicle to control its lateral positioning within the lane markings; *signaling* (operational maneuver), the proper use and timing of turn signals; *speed regulation* (operational or tactical maneuver), controlling the vehicle's speed in relation to the posted speed limit or flow of traffic; *vehicle positioning* (operational or tactical maneuver), controlling a safe buffer (e.g., 2 seconds) or distance in front and behind other vehicles; and *visual scanning* (operational maneuver), scanning the environment to detect or track information with head and eye movements (Classen et al., 2017; Justiss et al., 2006).

1.3.3 Determining Fitness to Drive

Through the CDE, the occupational therapist and licensed driving school instructor determine the driver's fitness based on driving history, habits, behaviours, skills, abilities, and/or actual on-road performance (Canadian Council of Motor Transport Administrators, 2020, p. 42-49; Classen et al., 2012, p. 221-277). This determination is based on whether the driver experiences visual, cognitive, sensory, and/or motor impairments that affect fitness to drive. Factors considered include the driver's insight and ability to compensate or accommodate for such impairments, and the driver's compliance with prescribed treatment or existing conditions (Canadian Council of Motor Transport Administrators, 2020, p. 42-49). The occupational therapist and licensed driving school instructor report their determination of the driver's fitness to the Ministry of Transportation of the various provinces. The Ministry of Transportation makes the final determination on the driver's fitness. Determinations include whether the driver is fit to drive and can continue to drive; requires accommodations (e.g., only drive in daylight hours), compensatory strategies (e.g., hand controls to compensate for lower limb impairment) or remedial strategies (e.g., turn head left and right to remediate peripheral field impairment); or is unfit to drive and should cease driving (Canadian Council of Motor Transport Administrators, 2020, p. 42-49).

1.3.4 Canadian Fitness to Drive Standards for Drivers with Multiple Sclerosis

Currently, the Canadian fitness to drive standards indicate that, among other populations (i.e., Parkinson's disease, cerebral palsy), drivers with MS are fit to drive if they meet the conditions to drive legally, and can physically and sufficiently operate a motor vehicle (Canadian Council of Motor Transport Administrators, 2020, p. 160). Alternatively, drivers must be able to compensate for any visual or motor losses, and cannot have cognitive impairments, pain, or medication that impair their driving ability (Canadian Council of Motor Transport Administrators, 2020, p. 160).

1.3.5 Limitations of the Comprehensive Driving Evaluation

The CDE most validly assesses fitness to drive, as it measures real-world driving performance in driving environments and under multiple conditions (Classen et al., 2012, p. 221-277; Di Stefano & Macdonald, 2012). However, the CDE poses challenges to drivers as it may be expensive, time consuming, and not easily accessible (Weaver & Bédard, 2012; Zou & Vu, 2019). Drivers referred to undergo a CDE may be required to conditionally cease driving until after their fitness to drive status has been determined, which may increase their anxiety and detrimentally affect their everyday activities (Caffò et al., 2020; College of Occupational Therapists, 2018; Ministry of Transportation of Ontario, 2018). Furthermore, the on-road assessment poses a crash risk, which increases risks to the health and safety of road users (Zou & Vu, 2019). Such drawbacks may make the CDE restrictive for medically at-risk drivers. Alternatively, computerized driving simulator assessments that target the underlying driving performance impairments of medically at-risk populations may feasibly inform clinicians' fitness to drive decisions (Allen et al., 2010; Campos et al., 2017).

1.4 Using Driving Simulators to Assess Driving Performance

Driving simulators enable drivers to interact with computerized representations of real-world driving scenarios (Allen et al., 2010; Campos et al., 2017). Depending on the purpose, driving simulators have different costs (e.g., $20K to more than $1M), configurations (e.g., desktop, partial cab, full cab), platforms (e.g., fixed-based, motion-based), visual displays (e.g., anterior, 360-degree field of view), and visual graphics (e.g., cartoon-based, photographic-based; Classen & Evans, 2017, p. 27-40). When using a driving simulator to assess driving performance in medically at-risk drivers, it is critical that the simulator's features and scenarios represent their underlying impairments of driving performance (Allen et al., 2010; Campos et al., 2017).

1.4.1 The Fidelity of Driving Simulators

Factors that may impact the validity of the driver's performance include the driving simulator's fidelity (Shechtman, 2010; Wynne et al., 2019). Fidelity refers to the level of the driving simulator's physical and psychological realism to real-world driving (Evans & Lavalliere, 2017, p. 67-82; Hirsch & Rosenthal, 2017, p. 75-83). Physical fidelity is the level of physical and sensory feedback of the driving simulator's equipment, environment, and scenarios that stimulate realistic visual, aural, inertial, and tactile senses (Evans & Lavallière, 2017, p. 67-82). Psychological fidelity, also known as presence, involves the driving simulator's equipment and scenarios to elicit realistic perception, interpretation, engagement, and driving behaviour (Hirsch & Rosenthal, 2017, p. 75-83). Scenarios that replicate interactive real-world driving tasks and environments that underlie deficits in driving performance may elicit realistic driving behaviours (Hirsch & Rosenthal, 2017, p. 75-83). Driving behaviours can be measured via objective kinematic or summary data collected by the driving simulator (e.g., mean speed), via driving assessors documenting the number and/or severity of driving errors, or via a combination of those methods (Society of Automotive Engineers International, 2015; Wynne et al., 2019).

Typically, more sophisticated driving simulators with features that represent those of a motor vehicle have higher levels of fidelity (Hirsch & Rosenthal, 2017, p. 75-83). However, these driving simulators tend to have limitations, such as higher upfront and maintenance costs, more space requirements, and an increased risk of experiencing simulator adaptation syndrome (SAS or simulator sickness; Stern et al., 2017, p. 107-120). Furthermore, driving simulators with desktop configurations can produce similar levels of fidelity without such limitations (Stern et al., 2017, p. 107-120). Thus, considering the driving simulator's costs, equipment, scenarios and features, in addition to the driver's limitations, may contribute to understanding one's driving behaviour when assessing driving performance on a simulator.

1.4.2 Benefits

When compared to on-road assessments, driving simulators have several advantages. For example, driving simulators do not have the risks associated with real-world driving (Classen & Evans, 2017, p. 34-35). Though the upfront costs of driving simulators may be high, today's technology enables lower maintenance and user costs (Classen & Evans, 2017, p. 34-35). Unlike on-road assessments that have unpredictable traffic and environmental conditions, manufacturers build driving simulator scenarios with controlled driving environments, tasks, and maneuvers; thus, enabling researchers to create highly reproducible assessments across time and participants (Classen & Evans, 2017, p. 34-35). Furthermore, manufacturers can modify the driving environments, tasks, and maneuvers of driving simulator scenarios to assist researchers in creating highly specific assessments that may target impairments related to a medically at-risk population, such as MS (Classen & Evans, 2017, p. 34-35). Such modifications can also enable researchers to create scenarios that safely assess drivers' crash risk or response to hazardous events (Classen & Evans, 2017, p. 34-35).

1.4.3 Limitations

Though driving simulators have several strengths, some limitations exist. The largest limitation may be the risk of experiencing SAS. According to sensory cue conflict theory, SAS may be due to the incongruency in ocular, motor, and kinesthetic systems when driving the simulator but not feeling the reactive forces as one would in real-life (Stern et al., 2017, p. 107-120). The cardinal symptoms may include dizziness, excessive salivating, eye strain, headache, nausea, pallor, restlessness, stomach irritation, sweating, and/or vomiting (Stern et al., 2017, p. 107-120). Though this possibility exists, empirical evidence supports mitigation protocols that prevent or alleviate the symptoms (Brooks et al., 2010; Stern et al., 2017, p. 107-120). Additionally, driving simulators do not measure real-world driving performance, and so driving simulator performance cannot be the sole source of information for making fitness to drive decisions (Wynne et al., 2019). However, valid driving performance measures can provide useful information about whether a CDE is warranted (Allen et al., 2010; Campos et al., 2017).

1.5 Clinical Indicators of On-Road Outcomes in Drivers with Multiple Sclerosis

1.5.1 Clinical Tests

In the literature, twelve studies document findings of clinical and on-road assessments for drivers with MS (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Classen et al., 2018; Devos et al., 2017; Krasniuk, Classen, Monahan, et al., 2019; Krasniuk et al., 2020; Krasniuk et al., 2017; Lincoln & Radford, 2008; Morrow et al., 2018; Schultheis et al., 2010; Schultheis et al., 2009). These study findings are summarized in Appendix A (p. 153-157). Table 1.1 summarizes the clinical tests included in each study, which mostly assessed for physical disability or cognitive impairment.

Table 1.1 Clinical Tests in On-Road Studies for Drivers with Multiple Sclerosis (*N* = 12 Studies)

Clinical Test	Study											
	1	2	3	4	5	6	7	8	9	10	11	12
Visual ability												
Colour perception[a,b]	X	—	—	X	X	—	—	—	—	—	—	—
Contrast sensitivity[a,b]	X	—	—	X	X	—	—	—	—	—	—	—
Depth perception[a,b]	X	—	—	X	X	—	—	—	—	—	—	—
Peripheral fields[a,b]	—	—	—	X	X	—	—	—	—	—	—	—
Phorias[b]	—	—	—	X	—	—	—	—	—	—	—	—
Visual acuity[a,b]	—	—	—	X	X	—	—	—	—	—	—	—
Cognitive ability												
Adult Memory and Information Processing Battery	—	—	—	—	—	—	—	—	X	—	—	—
Brief Visuospatial Memory Test-Revised Version	—	—	—	—	—	—	X	—	—	X	—	—
Controlled Oral and Word Association Test	—	—	—	—	—	—	—	—	—	X	—	—
California Verbal Learning Test-Second Edition	—	—	—	—	—	—	X	—	—	X	—	X
Delis-Kaplan Executive Function System-Sort Test	—	—	—	—	—	—	X	—	—	X	—	—
Judgement of Line Orientation	—	—	—	—	—	—	X	—	—	X	—	—
Mini-Mental State Exam	X	X	—	—	X	—	—	—	—	—	—	—
Motor-free Visual Perceptual Test-Revised Version	—	—	—	—	—	—	—	—	—	—	—	X
Paced Auditory Serial Addition Test	X	X	—	—	X	—	—	—	X	X	—	X
Rey-Osterrieth Complex Figure	X	—	—	—	X	—	—	—	—	—	—	
Symbol Digit Modalities Test	—	—	—	—	X	—	X	—	—	X	—	X
Stroke Driver Screening Assessment	X	X	X	—	X	—	—	—	X	—	—	
7/24 Spatial Recall Test	—	—	—	—	—	—	—	—	—	—	—	X
Stroop Colour and Word Test	X	—	X	—	X	—	—	—	X	—	—	—
Test of Motor Impersistence	—	—	—	—	—	—	—	—	X	—	—	—
Trail Making Test	X	—	—	—	X	—	—	—	—	—	—	X
Useful Field of View™	X	X	X	X	X	—	X	—	—	—	—	—
Wechsler Adult Intelligence Scale	X	—	—	—	—	—	—	—	—	—	—	X

Clinical Test	Study											
	1	2	3	4	5	6	7	8	9	10	11	12
Motor ability												
Barthel Index	X	X	—	—	X	—	—	—	—	—	—	—
Nine Hole Peg Test	X	—	—	—	X	—	—	—	—	—	—	—
Timed 25-Foot Walk	X	—	—	—	X	—	—	—	—	—	—	—
Physical Disability												
Expanded Disability Status Scale	X	X	—	X	X	—	—	—	—	X	X	—
Multiple Sclerosis Functional Composite	X	—	—	—	—	—	—	—	—	—	—	—

Note. X = included; — = not included.
Study: 1 = Akinwuntan, Devos, et al. (2012); 2 = Akinwuntan, O'Connor, et al. (2012); 3 = Akinwuntan et al. (2018); 4 = Classen et al. (2018); 5 = Devos et al. (2017); 6 = Krasniuk et al. (2017); 7 = Krasniuk, Classen, Monahan, et al. (2019); 8 = Krasniuk et al. (2020); 9 = Lincoln and Radford (2008); 10 = Morrow et al. (2018); 11 = Schultheis et al. (2009); 12 = (Schultheis et al., 2010).
[a]Keystone® Vision Screener; [b]OPTEC® 2500 Vision Screener.

1.5.2 On-Road Assessments

Table 1.2 summarizes the driving environments, maneuvers, and outcomes of on-road assessments included in each study (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Classen et al., 2018; Devos et al., 2017; Krasniuk, Classen, Monahan, et al., 2019; Krasniuk et al., 2020; Krasniuk et al., 2017; Lincoln & Radford, 2008; Morrow et al., 2018; Schultheis et al., 2010; Schultheis et al., 2009). During these on-road assessments, drivers performed operational and/or tactical maneuvers in residential, suburban, urban, and highway environments. One study also included a strategic driving maneuver that involved navigating and wayfinding ability to assess a busy parking lot and choose an exit based on the choice available in an urban environment (Krasniuk, Classen, Monahan, et al., 2019).

Driving outcomes included a global rating score (e.g., pass vs. fail) and/or the number and total of driving errors in adjustment to stimuli, gap acceptance, lane maintenance, signaling, speed regulation, vehicle positioning, and/or visual scanning. One study included the total scores in operational (e.g., lateral lane position), tactical (e.g., speed adaptation), visual-integrative (e.g., anticipation and perception of road signs), and mixed maneuvers (e.g., merging; Devos et al., 2017).

Table 1.2 Components of On-Road Assessments for Drivers with Multiple Sclerosis (*N* = 12 Studies)

On-Road Components	Study											
	1	2	3	4	5	6	7	8	9	10	11	12
Environment												
Residential	X	X	X	X	X	X	—	X	X	X	X	X
Suburban	X	X	X	X	X	X	—	X	X	X	X	X
Urban	X	X	X	X	X	X	X	X	X	X	X	X
Highway	X	X	X	X	X	X	—	X	X	X	X	X
Maneuver												
Adjust to stimuli	X	X	X	X	X	X	X	X	X	X	X	X
Gap acceptance	X	X	X	X	X	X	X	X	X	X	X	X
Lane maintenance	X	X	X	X	X	—	X	—	X	X	X	X
Signaling	X	X	X	X	X	—	X	—	X	X	X	X
Speed regulation	X	X	X	X	X	—	X	—	X	X	X	X
Vehicle positioning	X	X	X	X	X	—	X	—	X	X	X	X
Visual scanning	X	X	X	X	X	—	X	—	X	X	X	X
Outcome												
Global rating	X	X	X	X	—	X	X	X	X	X	X	X
Driving errors (no.)												
Total	—	—	X	X	X	X	X	X	—	—	—	—
Adjust to stimuli	—	—	—	X	X	X	X	X	—	—	—	—
Gap acceptance	—	—	—	X	X	X	X	X	—	—	—	—
Lane maintenance	—	—	—	X	X	—	X	—	—	—	—	—
Signaling	—	—	—	X	X	—	X	—	—	—	—	—
Speed regulation	—	—	—	X	X	—	X	—	—	—	—	—
Vehicle positioning	—	—	—	X	X	—	X	—	—	—	—	—
Visual scanning	—	—	—	X	X	—	X	—	—	—	—	—

Note. X = included; — = not included.
Study: 1 = Akinwuntan, Devos, et al. (2012); 2 = Akinwuntan, O'Connor, et al. (2012); 3 = Akinwuntan et al. (2018); 4 = Classen et al. (2018); 5 = Devos et al. (2017); 6 = Krasniuk et al. (2017); 7 = Krasniuk, Classen, Monahan, et al. (2019); 8 = Krasniuk et al. (2020); 9 = Lincoln and Radford (2008); 10 = Morrow et al. (2018); 11 = Schultheis et al. (2009); 12 = Schultheis et al. (2010).

1.5.3 Findings

Overall, 15% to 40% of drivers with MS failed the on-road assessment (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Classen et al., 2018; Krasniuk, Classen, Monahan, et al., 2019; Krasniuk et al., 2020; Krasniuk et al., 2017; Lincoln & Radford, 2008; Morrow et al., 2018; Schultheis et al., 2010; Schultheis et al., 2009). Driving errors that indicated failing outcomes included the number of adjustment to stimuli errors (operational or tactical maneuvers) and gap acceptance errors (tactical maneuvers), particularly in suburban and urban environments;

and the number of lane maintenance errors and speed regulation errors of a strategic driving maneuver (Classen et al., 2017; Classen et al., 2018; Krasniuk, Classen, Monahan, et al., 2019; Krasniuk et al., 2020; Krasniuk et al., 2017).

Furthermore, consistent findings showed six visual-cognitive tests to predict failing outcomes. These tests included the: Adult Memory and Information Processing Battery (Task B, Design Learning), Immediate Recall Measure of the Brief Visuospatial Memory Test-Revised Version (BVMTR-IR), Stroke Driver Screening Assessment, Stroop Colour and Word Test, Symbol Digit Modalities Test-Oral Version (SDMT), and the central visual processing speed subtest of the Useful Field of View™ (UFOV1; Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Devos et al., 2017; Lincoln & Radford, 2008; Morrow et al., 2018; Schultheis et al., 2010).

Three clinical tests also correlated with driving errors that indicated failing outcomes: losses in far-sighted binocular visual acuity on the OPTEC® 2500 Vision Screener correlated with a higher number of adjustment to stimuli errors; slower central visual processing speed on the UFOV1 correlated with a higher number of gap acceptance errors; and decreases in delayed visuospatial recall on the BVMTR (BVMTR-DR) correlated with a higher number of speed regulation errors of a strategic driving maneuver (Classen et al., 2018; Krasniuk, Classen, Monahan, et al., 2019).

Overall, these findings show that impairment in far-sighted visual acuity, complex attention (e.g., divided, sustained), executive function (e.g., reasoning), information processing speed, visuospatial ability, and working memory may underlie driving performance deficits in drivers with MS. Adjustment to stimuli errors (operational or tactical maneuvers), gap acceptance errors (tactical maneuver), and those of a strategic driving maneuver, in suburban and urban environments, may detect driving performance deficits.

1.6 Clinical Indicators of Driving Simulator Outcomes in Drivers with Multiple Sclerosis

1.6.1 Clinical Tests

In comparison to on-road studies, six driving simulator studies document findings of clinical and driving simulator assessments for drivers with MS (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003; Lamargue-Hamel et al., 2015; Marcotte et al., 2008; Raphail et al., 2020). The findings of these studies are summarized in Appendix B (p. 158-161). Table 1.3 summarizes the clinical tests included in each study, which mostly assessed for physical disability, motor impairment, or cognitive impairment.

Table 1.3 Clinical Tests in Driving Simulator Studies for Drivers with Multiple Sclerosis (*N* = 6 Studies)

Clinical Test	Study					
	1	2	3	4	5	6
Visual ability						
Contrast sensitivity[a]	X	—	—	—	—	—
Visual acuity[b]	X	—	—	—	—	—
Cognitive ability						
Baddeley Double Task	—	—	—	X	—	—
California Verbal Learning Test	—	—	—	X	—	—
Hopkins Verbal Learning Test, Revised Version	—	—	—	—	X	—
Mini Mental Status Exam	—	—	—	X	—	—
Naming Task	—	—	—	X	—	—
Paced Auditory Serial Addition Test	X	—	X	—	X	X
Repeatable Battery Assessment for Neurological Status	X	—	—	—	—	—
Reverse Span	—	—	—	X	—	—
Rey-Osterrieth Complex Figure	—	—	—	X	—	—
Symbol Digit Modalities Test	—	X	—	X	—	—
Stroke Driver Screening Assessment	X	—	—	—	—	—
Stroop Colour and Word Test	—	—	—	X	—	—
Test of Attentional Performance	—	X	—	X	—	—
Trail Making Test	X	—	—	X	X	X
Verbal fluency	—	—	—	X	—	—
Wechsler Adult Intelligence Scale	—	—	—	—	X	—
Motor ability						
Functional Reach Test	X	—	—	—	—	—
Grooved Pegboard Test	—	—	—	—	X	—
Modified Ashworth Test	X	—	—	—	X	—
Motricity Index	X	—	—	—	—	—

Clinical Test	Study					
	1	2	3	4	5	6
Nine Hole Peg Test	X	—	X	—	—	X
Timed 25-Foot Walk	X	—	X	—	—	X
Physical Disability						
Expanded Disability Status Scale	X	—	X	X	X	X
Multiple Sclerosis Functional Composite	—	—	X	—	—	X

Note. X = included; — not included.
Study: 1 = Devos et al. (2013); 2 = Harand et al. (2018); 3 = Kotterba et al. (2003); 4 = Lamargue-Hamel et al. (2015); 5 = Marcotte et al. (2008); 6 = Raphail et al. (2020).
[a]Pelli-Robson Chart; [b]Armaignac Chart.

1.6.2 Driving Simulator Assessments

Table 1.4 summarizes the driving environments, maneuvers, and outcomes of driving simulator scenarios in each study. In most scenarios, drivers completed operational maneuvers in highway environments. Notably, drivers maintained a constant speed and lane positioning during monotonous drives (Devos et al., 2013; Harand et al., 2018; Lamargue-Hamel et al., 2015; Marcotte et al., 2008; Raphail et al., 2020). Some scenarios also required drivers to respond to stimuli during secondary driving tasks (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003).

In three studies, drivers completed tactical maneuvers, such as overtaking other vehicles or judging and responding to hazardous events to avoid collisions (e.g., hidden pedestrian crossing; Devos et al., 2013; Harand et al., 2018; Marcotte et al., 2008). Lastly, in one study, drivers completed a strategic driving maneuver via responding to an overtaking emergency vehicle (Devos et al., 2013).

As displayed in Table 1.4, driving outcomes mostly comprised summary measures (e.g., *M*, *SD*) that indicated errors in adjustment to stimuli, lane maintenance, speed regulation, and/or visual scanning throughout trials or the duration of the scenario (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003; Lamargue-Hamel et al., 2015; Marcotte et al., 2008; Raphail et al., 2020).

Table 1.4 Components of Driving Simulator Scenarios for Drivers with Multiple Sclerosis (*N* = 6 Studies)

Simulator Scenario Components	Study					
	1	2	3	4	5	6
Environment						
Residential	—	—	—	—	—	—
Suburban	—	—	—	—	—	—
Urban	X	X	—	—	—	—
Highway	X	X	X	X	X	X
Maneuver						
Adjust to stimuli	X	X	X	X	X	—
Gap acceptance	X	X	—	—	—	—
Lane maintenance	X	X	—	—	X	X
Signaling	—	—	—	—	—	—
Speed regulation	X	X	X	X	X	X
Vehicle positioning	X	X	—	—	X	—
Visual scanning	X	X	X	—	X	—
Outcome						
Adjust to stimuli (*no*. crashes, *no.* traffic tickets, response time, and/or response accuracy)	X	X	X	—	X	—
Gap acceptance (time to collision)	X	—	—	—	—	—
Lane maintenance (*M*, *SD*, and/or *variability* in lateral lane positioning, and/or *no.* lane crossings)	X	X	—	X	X	X
Signaling	—	—	—	—	—	—
Speed regulation (*M*, *SD*, and/or *variability* in speed)	X	X	—	X	X	X
Vehicle positioning (coherence, modulus, time delay)	—	—	—	—	X	—
Visual scanning (response time and/or response accuracy)	X	X	X	—	X	—

Note. X = included; — not included.
Study: 1 = Devos et al. (2013); 2 = Harand et al. (2018); 3 = Kotterba et al. (2003); 4 = Lamargue-Hamel et al. (2015); 5 = Marcotte et al. (2008); 6 = Raphail et al. (2020).

1.6.3 Findings

Findings showed that when compared to drivers without MS, those with MS had slower response time or reaction time, poorer response accuracy, greater speed and lane variability, made more errors, and had higher crash rates (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003; Lamargue-Hamel et al., 2015; Marcotte et al., 2008). For drivers with MS, impairment in auditory information processing speed, working memory, and divided attention correlated with greater speed variability or higher crash rates (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003). Overall, these findings indicate that losses in auditory information processing speed, divided attention, and working memory may underlie driving performance deficits on a driving simulator in those with MS. Furthermore, simulated operational adjustment to stimuli errors during highway drives may detect decreases in driving performance.

1.7 Gaps in the Literature

1.7.1 Clinical Tests that Underlie Driving Performance Deficits

The findings in the literature identify three gaps that make it difficult to understand if a driving simulator can measure driving performance deficits in those with MS. First, on-road and driving simulator studies show inconsistent findings for which visual and cognitive impairments indicate deficits in driving performance. On-road studies show that impairment in visual acuity, complex attention, executive function, information processing speed, visuospatial ability, and working memory underlie driving performance impairment (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Classen et al., 2018; Krasniuk, Classen, Monahan, et al., 2019; Lincoln & Radford, 2008; Morrow et al., 2018; Schultheis et al., 2010).

When compared to on-road studies, driving simulator studies include tests that measure the same cognitive domains: i.e., *complex attention* (Devos et al., 2013; Lamargue-Hamel et al., 2015; Marcotte et al., 2008; Raphail et al., 2020), *executive function* (Devos et al., 2013; Lamargue-Hamel et al., 2015; Marcotte et al., 2008; Raphail et al., 2020), *information processing speed* (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003; Lamargue-Hamel et al., 2015; Marcotte et al., 2008; Raphail et al., 2020), *visuospatial ability* (Devos et al., 2013; Lamargue-Hamel et al., 2015), and *working memory* (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003; Lamargue-Hamel et al., 2015; Marcotte et al., 2008; Raphail et al., 2020). Furthermore, three driving simulator studies included visual or cognitive tests that on-road studies found to indicate driving outcomes (Devos et al., 2013; Harand et al., 2018; Lamargue-Hamel et al., 2015). The tests included the *Stroke Driver Screening Assessment* (Devos et al., 2013), *Stroop Colour and Word Test* (Lamargue-Hamel et al., 2015), *SDMT* (Harand et al., 2018; Lamargue-Hamel et al., 2015), and an assessment of *visual acuity* (Devos et al., 2013). However, study findings showed auditory information processing speed, divided attention, and working memory to indicate driving simulator performance in drivers with MS (Devos et al., 2013; Harand et al., 2018; Lamargue-Hamel et al., 2015). Whether the same visual and cognitive impairments and clinical tests that underlie deficits in on-road outcomes can also underlie deficits in driving simulator outcomes is not fully understood.

1.7.2 Driving Maneuvers, Errors, and Environments that Indicate Driving Performance Deficits

Second, on-road and driving simulator study findings consistently show that adjustment to stimuli errors may underlie driving performance impairment in drivers with MS (Classen et al., 2017; Classen et al., 2018; Devos et al., 2013; Devos et al., 2017; Harand et al., 2018; Kotterba et al., 2003; Krasniuk et al., 2020; Krasniuk et al., 2017). However, on-road studies document driving errors as the total number throughout the entire on-road assessment or per environment (e.g., suburban, urban). In comparison, driving simulator studies document the drivers' operational maneuvers when responding to stimuli across trials or throughout the duration of a highway drive, and not often in suburban or urban environments (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003).

Overall, these findings make it difficult to understand whether operational and/or tactical adjustment to stimuli errors can indicate driving performance impairment in drivers with MS; and whether such errors can be detected in suburban and/or urban environments of a simulated scenario. Understanding if such simulated maneuvers, errors, and environments can detect driving performance impairment in drivers with MS may help develop targeted driving simulator assessments that may be used to inform fitness to drive decisions.

1.7.3 Feasibility of Utilizing Clinical Tests to Detect Driving Simulator Performance

Third, the feasibility of utilizing clinical tests to detect driving simulator performance in drivers with MS is not well studied. Feasibility is important for understanding the advantages, challenges, practicability, and capability of implementing a study based on participant recruitment methods, data collection procedures, outcome measures, participants' acceptability and suitability of testing procedures, resources required to manage and implement the study, and preliminary test results (Orsmond & Cohn, 2015).

Based on the existing literature, little is understood about challenges with recruitment (e.g., low recruitment rates), data collection procedures and outcome measures (e.g., simulator malfunctions), participants’ acceptability (e.g., perceptions on simulator’s usefulness or usability) or suitability toward the driving simulator (e.g., occurrence of SAS), or the resources and management required to implement the study (e.g., costs). Determining the feasibility may provide insight to the challenges of driving simulator assessments for drivers with MS, including confounding variables that may affect driving performance such as the occurrence of SAS.

1.8 Dissertation Rationale

The rationale for this study derives from three fronts. First, because the feasibility of utilizing clinical tests to indicate driving simulator performance in drivers with MS is not well studied, little is understood about the challenges associated with driving studies or driving simulators that can impact participation and adherence rates, complete data collection, and test results. Accordingly, this dissertation will examine this gap in the literature. Understanding the feasibility of the study will indicate the advantages, challenges, practicability, and capability of factors that may impact study findings and whether to execute a full-scale study.

Second, the inconsistency between on-road and driving simulator study findings for which visual and cognitive impairment can indicate driving performance deficits identifies the need to determine whether the same clinical tests found to underlie on-road driving performance can also underlie driving performance on a driving simulator. Understanding this gap in the literature may provide insight to whether driving simulator assessments may be used as a substitute to assess fitness to drive in people with MS.

Third, the inconsistency between on-road and driving simulator study findings for which driving maneuvers, environments, and errors can detect driving performance impairment in drivers with MS make it difficult to understand if such errors can be detected on a driving simulator. Understanding whether operational and/or tactical adjustment to stimuli errors in suburban and/or urban environments can indicate driving simulator performance impairment in drivers with MS may guide fitness to drive decision-making.

1.9 Objectives, Aims, and Hypotheses

Based on prior on-road study findings (Classen et al., 2017; Classen et al., 2018; Krasniuk, Classen, Monahan, et al., 2019; Krasniuk et al., 2020; Krasniuk et al., 2017; Morrow et al., 2018), this dissertation will examine the clinical utility of visual and cognitive tests to indicate driving simulator performance in drivers with MS, when compared to control drivers without MS. The dissertation has three aims.

The first aim will examine the feasibility of the study via evaluating: 1) Recruitment capability and resulting sample characteristics; 2) Data collection procedures and outcome measures; 3) The acceptability and suitability of the driving simulator; 4) The resources and ability to manage and implement the study; and 5) Preliminary clinical and driving simulator test results (see Chapter 2, p. 34-82). Feasibility findings will indicate the suitability to execute a full-scale study to quantify the clinical tests that predict driving performance.

Based on feasibility findings in the first aim, the second aim will examine if the clinical tests (BVMTR-IR, BVMTR-DR, CVLT2-IR, SDMT, UFOV, and far-sighted binocular visual acuity) can detect operational, tactical, and/or strategic errors on a driving simulator in drivers with MS, when compared to control drivers without MS (see Chapter 3, p. 83-102). At least one of these clinical tests predict decreased on-road outcomes in drivers with MS (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Classen et al., 2018; Devos et al., 2017; Krasniuk, Classen, Monahan, et al., 2019; Morrow et al., 2018; Ranchet et al., 2015; Schultheis et al., 2010). Accordingly, it is hypothesized that impairment in at least one clinical test will predict simulated driving errors in drivers with MS. Predictive findings will show if visual and/or cognitive deficits are suitable for making determinations about one’s driving performance.

Lastly, the third aim will examine if adjustment to stimuli errors can detect the occurrence of rear-end collisions on a driving simulator in drivers with MS, when compared to drivers without MS (see Chapter 4, p. 103-120). As on-road study findings show that adjustment to stimuli errors indicate drivers with MS failing an on-road assessment (Classen et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2017), it is hypothesized that simulated adjustment to stimuli errors will predict simulated rear-end collisions in drivers with MS. Predictive findings will show if adjustment to stimuli errors, which underlie on-road driving performance deficits, can be detected on a driving simulator.

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Chapter 2

2 Feasibility of Utilizing Clinical Tests to Predict Driving Simulator Performance in Drivers with Multiple Sclerosis

In the literature, six studies have documented clinical tests that can detect driving simulator performance in drivers with MS (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003; Lamargue-Hamel et al., 2015; Marcotte et al., 2008; Raphail et al., 2020). Study findings showed that, when compared to drivers without MS, drivers with MS have slower response time and poorer response accuracy during simulated divided attention tasks, and drive faster with greater speed and lane variability during simulated monotonous highway drives (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003; Marcotte et al., 2008). Furthermore, impairment in auditory processing speed, divided attention, and working memory may impact driving simulator performance (Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003). However, the visual-cognitive impairment that underlie driving maneuver deficits on a driving simulator is not fully understood. Therefore, this study will examine the gap in the literature.

In a prior on-road study, adjustment to stimuli errors (operational or tactical), gap acceptance errors (tactical), and those underlying a strategic driving maneuver pertaining to navigation and wayfinding ability indicated failing an on-road assessment in drivers with MS (Classen, Krasniuk, et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2019; Krasniuk et al., 2017). Impairment in far-sighted binocular visual acuity, central visual processing speed, visual information processing speed, working memory, and immediate and delayed visuospatial recall detected failing outcomes (Classen, Krasniuk, et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2019; Krasniuk et al., 2017; Morrow et al., 2018). Based on the prior study findings, this study will examine if the same driving errors and visual-cognitive impairment underlie driving simulator performance deficits in drivers with MS. But, because driving simulator studies reveal little findings on feasibility, the research student is undertaking the task prior to the prediction studies.

The study will not include an intervention, but it will address foundational components that may guide and inform the development of future interventions (Orsmond & Cohn, 2015). Accordingly, examining the study's feasibility will provide information pertaining to the following components: 1) recruiting eligible participants with similar demographic characteristics to the MS population-based sample within the planned timeframe; 2) the adequacy of data collection procedures and outcome measures for participants; 3) participants' perceptions toward using the driving simulator and whether the onset of SAS affects completing the simulated scenarios; 4) obtaining the resources and ability to conduct the study successfully as per the protocol; and 5) preliminary test results that identify potential clinical indicators of driving performance in drivers with MS (Orsmond & Cohn, 2015). If the study findings confirm feasibility, it will lay the foundation for executing a full-scale study to quantify the clinical tests that predict driving performance (Orsmond & Cohn, 2015). Understanding if driving performance deficits that contribute to on-road outcomes can be detected on a driving simulator is important for making valid decisions about one's driving performance.

2.1 Objective

This study will examine the feasibility of utilizing visual and cognitive clinical tests to indicate driving simulator performance in drivers with MS, when compared to drivers without MS.

2.2 Aims

This study will examine feasibility via a framework with five aims: 1) Evaluate recruitment capability and resulting sample characteristics; 2) Evaluate data collection procedures and outcome measures; 3) Evaluate the acceptability and suitability of the driving simulator; 4) Evaluate the resources and ability to manage and implement the study; and 5) Evaluate preliminary clinical and driving simulator test results (Orsmond & Cohn, 2015).

2.3 Methods

2.3.1 Ethics

Lawson's Health Research Institute (R-18-631) and the University of Western Ontario's Health Sciences Research Ethics Board (112525) approved this research study (see Appendix C, p. 162-163). All participants with MS and without MS consented in writing to take part in the study. Participants received a $25 CAD gift card for their time and commitment.

2.3.2 Design

Feasibility study informed by the Orsmond and Cohn (2015) Framework.

2.3.3 Participant Recruitment

Participant recruitment occurred between January 2019 and February 2020 in London, Ontario, Canada. Convenience sampling methods included recruiting through advertising in the London (Ontario) MS Clinic, University of Western Ontario, and MS Society of Canada's Research Portal; and via recruiting online advertisements on social media or network sites (i.e., Kijiji, Craigslist), and in online editions of local newspapers.

2.3.4 Inclusion and Exclusion Criteria

Inclusion criteria were participants, 18 to 59 years, with a valid graduated driver's license, who met the legal vision standards to drive in Ontario (Ministry of Transportation of Ontario, 2018). The legal vision standards include a corrected or uncorrected, far-sighted binocular visual acuity of at least 20/50 and binocular horizontal field of view of at least 120 degrees continuous (Ministry of Transportation of Ontario, 2018). Participants with MS had a physician-verified diagnosis (Lublin et al., 2014; Thompson et al., 2018), and low to moderate physical disability on the Expanded Disability Status Scale (EDSS) with a score between 0 and 6.5 (Kurtzke, 1983).

Exclusion criteria were based on the neurologists' findings and pertained to: participants who had other physician-verified medical, neurological, or psychiatric diagnoses that could affect performance on the study measures; took medications or illicit drugs that potentially impacted cognitive or driving ability; experienced relapses or had corticosteroid treatment three months prior to study enrolment; experienced severe fatigue as per the Fatigue Severity Scale (*M* score >5; Krupp et al., 1989); and/or experienced severe depression on the Beck Depression Index Fast Screen (*total* score ≥14; Beck, Steer, & Brown, 2000).

2.3.5 Procedure

Participants attended one in-person visit at the University of Western Ontario's i-Mobile Driving Research Lab, located in the School of Occupational Therapy. Upon obtaining written informed consent, the research student screened participants to confirm they met all the inclusion and exclusion criteria. Participants completed a standardized demographic and medical intake form (Classen et al., 2008), Driver Behaviour Questionnaire (Cordazzo et al., 2014; Reason et al., 1990), and a clinical assessment battery of standardized visual and cognitive tests that previously indicated failing an on-road assessment in drivers with MS (Classen, Krasniuk, et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2019; Krasniuk et al., 2017; Morrow et al., 2018). The clinical assessment included the BVMTR-IR, BVMTR-DR, CVLT2-IR, SDMT, UFOV, and an assessment of far-sighted binocular visual acuity (Benedict, 1997; Benedict et al., 2012; Delis et al., 2000; Langdon et al., 2012; Rao, 1991; Stereo Optical Inc., 2017; Visual Awareness Research Group, 2009). The trained research student administered the testing battery, which took approximately one hour to complete.

After the clinical assessment, participants completed a driving simulator assessment with a SAS mitigation protocol (see p. 42), and a main driving scenario (see p. 44-51), which was previously designed, tested, refined, and validated to detect adjustment to stimuli errors and visual scanning errors of youth drivers (Alvarez et al., 2019; Alvarez, Classen, Medhizadah, Knott, Asantey, et al., 2018; Alvarez, Classen, Medhizadah, Knott, & He, 2018). The research student selected this driving scenario to assess participants' adjustment to stimuli (operational, tactical) and strategic driving maneuvers that targeted driving performance deficits in drivers with MS, as adjustment to stimuli errors and strategic errors of a navigational driving task previously indicated failing an on-road assessment (Classen, Krasniuk, et al., 2017; Classen et al., 2018; Krasniuk et al., 2020;

Krasniuk et al., 2019; Krasniuk et al., 2017; Morrow et al., 2018). The trained research student administered the driving simulator assessment, which lasted for approximately 30 minutes. Participants had rest breaks as needed.

2.3.6 Measures

2.3.6.1 Intake Form

Participants reported demographic and medical information on a standardized intake form (e.g., age, sex, ethnic origin, education, employment, number and type of medications, and medical conditions or comorbidities). The intake form was developed and standardized to detect on-road outcomes in older drivers (Classen et al., 2008), but the form has also been used in neurological populations, e.g., those with Parkinson's disease (Alvarez & Classen, 2018). The research student adapted the form to document MS-related information, such as type of MS, years since diagnosis, and years since most recent relapse.

2.3.6.2 Driver Behaviour Questionnaire

The North American Driver Behaviour Questionnaire is widely used to measure self-reported driving behaviours in several populations (Cordazzo et al., 2014; Reason et al., 1990). Linked to crash risk and traffic violations, relative validity exists between the Driver Behaviour Questionnaire and on-road or driving simulator performance (Helman & Reed, 2015; Zhang et al., 2013; Zhao et al., 2012). The 50-item questionnaire uses a six-point Likert scale (0-5, never to nearly all the time) to report on the frequency of committing slips which are failed planned actions, violations which are deviations from practices necessary for operating a vehicle, and mistakes which are unwitting deviations of action (Cordazzo et al., 2014; Reason et al., 1990). For this study, the research student averaged participants' responses on slips, violations, and mistakes.

2.3.6.3 Clinical Assessment

2.3.6.3.1 OPTEC® 5000 Peripheral-Glare Vision Screener

The OPTEC® 5000 Peripheral-Glare Vision Screener is a light-emitting diode system that measures various near-sighted (i.e., 16 inches) or far-sighted (i.e., 20 feet) visual ability, through monocular or binocular vision, under day or night, and glare or no glare settings (Stereo Optical Inc., 2017). For this study, the research student assessed far-sighted binocular visual acuity in daytime and no glare conditions. Like the Snellen visual acuity chart, the OPTEC® visual acuity subtest measures participants' binocular visual acuity through reading letters in seven rows on a chart (Stereo Optical Inc., 2017). In the vision screener, the size of the letters in each row simulates a person's visual acuity at 20 feet (i.e., numerator) compared to the standardized visual acuity distance (i.e., denominator; Stereo Optical Inc., 2017). For example, the first row simulates a person's visual acuity at 20 feet compared to a standardized visual acuity at 200 feet. The last row simulates a visual acuity of 20/20. Test scores included the furthest row down out of seven rows that had less than two errors. The research student selected the OPTEC® visual acuity subtest (vs. Snellen visual acuity chart) because losses in visual acuity measured with the subtest correlated with more adjustment to stimuli errors in 29 drivers with MS (r_s = .5, p = .006; Classen et al., 2018).

2.3.6.3.2 Useful Field of View™

The UFOV is a 15-minute, computerized test with three subtests. The first subtest, UFOV1, measures central visual processing speed (Visual Awareness Research Group, 2009). The visual depiction of the test occurs on a single computer monitor screen and requires the participant to distinguish between a car or truck in the center of the screen (Visual Awareness Research Group, 2009). The second subtest, UFOV2, measures divided attention and visual processing speed through completing the tasks in UFOV1 and identifying an object located in the periphery of the screen (Visual Awareness Research Group, 2009). The third subtest, UFOV3, measures selective attention and visual processing speed through completing the UFOV2 while ignoring distractors found in the center and periphery of the screen (Visual Awareness Research Group, 2009). For each subtest, test scores included the mean response accuracy in milliseconds based on accurately responding to 75% of items presented (Visual Awareness Research Group, 2009).

The research student selected the UFOV because the test is recommended to individuals with cognitive impairment—thus, fitting for individuals with MS (Visual Awareness

Research Group, 2009). Previous research showed that slower central visual processing speed on UFOV1 correlated with more gap acceptance errors in 29 drivers with MS (r_s = .4, p = .03; Classen et al., 2018). Also, two studies showed that when modelled with other visual-cognitive tests, the UFOV1 has predictive validity for detecting on-road outcomes in drivers with MS, with at least 80% accuracy (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012).

2.3.6.3.3 Brief International Cognitive Assessment for MS

The Brief International Cognitive Assessment for Multiple Sclerosis consists of the SDMT, CVLT2-IR, and BVMTR-IR—all standardized, psychometrically sound, and highly ranked neurological tests of visual and auditory information processing speed and memory (Benedict et al., 2012; Delis et al., 2000; Langdon et al., 2012). The SDMT measures participants' visual information processing speed and working memory by interpreting and reading the symbols' paired numbers in a 90-second interval (Rao, 1991). Test scores included the number of correct responses in 90 seconds.

The CVLT2-IR measures participants' immediate verbal/auditory recall through five trials of recalling words on an itemized list (Delis et al., 2000). Test scores included the number of correct responses across five trials out of 80.

The BVMTR-IR measures participants' immediate visuospatial recall through three trials of recalling and drawing six geometric figures in their locations on a display (Benedict, 1997). Each figure recalled receives zero to two points, depending on the accuracy and location of the figure on the testing form (Benedict, 1997). Test scores included the number of correct responses across three trials out of 36.

The research student selected the Brief International Cognitive Assessment for Multiple Sclerosis because the SDMT and BVMTR-IR previously predicted on-road outcomes in 35 drivers with MS with 100% sensitivity, 54% specificity, 38 positive and 100% negative predictive values, 36% misclassified, and 46% error rate ($x^2(df = 1, N = 36) = 7.3, p = .007$; Morrow et al., 2018).

2.3.6.3.4 Brief Visuospatial Memory Test-Revised Version, Delayed Recall Measure

To ensure an assessment of delayed recall, the BVMTR-DR occurred 20 minutes after the BVMTR-IR (Benedict, 1997). Test scores included the number of correct responses in one trial out of 12 based on the accuracy and location of the six figures on the testing form. The research student selected the BVMTR-DR because decreases in delayed visuospatial recall previously correlated with driving errors of a strategic driving maneuver in 35 drivers with MS ($r_s = -.4$, $p < .05$; Krasniuk et al., 2019).

2.3.6.4 Driving Simulator Assessment

2.3.6.4.1 CDS 200 Simulator

The driving simulator assessment occurred on the medium-fidelity CDS 200 DriveSafety™ Simulator (DriveSafety™, 2017; Stern, Swanepoel, et al., 2017, p. 48). As illustrated in Figure 2.1, the driving simulator had basic driver controls, including the steering wheel, signal indicators, accelerator and brake pedals, as well as an adjustable electric lift table and rear and side view wide-angle mirrors (DriveSafety™, 2017). The computer desktop model with a fixed-based platform included three 19-inch LCD screens, each with 1920 by 1080 resolution, that covered the anterior part of the drive over a 110-degree horizontal field of view (DriveSafety™, 2017).

Figure 2.1 CDS 200 DriveSafety™ Simulator by DriveSafety, Inc. (https://drivesafety.com). Reprinted with permission.

2.3.6.4.2 Simulator Adaptation Syndrome Mitigation Protocol

As part of a protocol for mitigating symptoms of SAS (Brooks et al., 2010; Stern, Akinwuntan, et al., 2017, p. 107-120), the research student asked participants to refrain from alcohol, caffeine, high-fat, or any mind-altering substance intake 24 hours prior to the study visit (Brooks et al., 2010; Stern, Akinwuntan, et al., 2017, p. 107-120). The simulator lab was set up according to the SAS mitigation protocol (Brooks et al., 2010; Stern, Akinwuntan, et al., 2017, p. 107-120). For example, the room had an exclusive air conditioning unit, with a room temperature of 72 degrees Fahrenheit (22 degrees Celsius). A tower fan ensured consistent air flow throughout the room. The dim light settings reduced glare from the simulator's screen monitors. The research student first oriented participants to the driving simulator's controls, and then calibrated and adjusted the driver controls to meet participants' anthropometric measures (Alvarez et al., 2019; Alvarez, Classen, Medhizadah, Knott, Asantey, et al., 2018; Alvarez, Classen, Medhizadah, Knott, & He, 2018).

The research student established baseline SAS measures with the Modified Motion Sickness Assessment Questionnaire (Brooks et al., 2010). Before and after each drive, participants reported if they experienced symptoms of SAS (e.g., sweaty, queasy, dizzy, nauseous) on an 11-point ordinal scale (0-10, not at all to severely) and the research student documented their scores on the questionnaire (Brooks et al., 2010). A cut-point of five indicated to immediately terminate the assessment due to SAS. Soda crackers, ginger ale, and water were available if participants experienced any discomfort. Participants were offered breaks, or to walk outside, allowing them to return to baseline conditions prior to resuming continued simulated driving.

2.3.6.4.3 Pre-Driving Exercises

As part of the SAS mitigation protocol, participants completed two one-minute pre-driving exercises to practice operating and controlling the steering wheel, accelerator, and brake pedals. The first pre-drive involved turning the steering wheel in the direction of a static target zone and maintaining the steering wheel's position in the zone for two seconds. The second pre-drive involved pressing the accelerator or brake pedal until the indicator was in the static target zone and maintaining the indicator's position in the zone for three seconds. For both pre-drives, the driving simulator recorded the number of correct responses and displayed the results on the screen for participants to view. Participants repeated the pre-drives if they needed to adjust the driver controls.

2.3.6.4.4 Adaptation Drives

After the pre-driving exercises, participants completed three adaptation drives (approximately 7 minutes total) to practice driving up to 50 kilometers per hour (31 miles per hour, 13.9 meters per second) and stopping or turning on residential, suburban, or urban roads with other road users. Each adaptation drive progressed in task complexity. Furthermore, the protocol was part of mitigating SAS, with the first adaptation drive having the least risk, and the last adaptation drive having the highest risk of experiencing SAS (Stern, Akinwuntan, et al., 2017, p. 107-120).

The first adaptation drive involved lane keeping skills while traveling straight and stopping on a two-lane rural road with no simulated road users. Participants had to maintain in their lane, while driving straight with a constant speed of 50 kilometers per hour (31 miles per hour, 13.9 meters per second) for 30 seconds. If participants experienced difficulty, the research student reminded them to follow the drive's directions. The drive ended once participants successfully followed the directions of the drive. Subsequently, participants completed the second and then third adaptation drives.

The second adaptation drive involved completing four left turns at traffic lights or stop signs on two-lane residential roads or two- to four-lane suburban roads. While driving in light traffic conditions, with a continuous flow of traffic, participants had to turn left when they received verbal and visual directions (i.e., directional arrow on the monitor screen) from the driving simulator. If participants experienced difficulty, such as missed the lane markings, the research student cued them to take the turns at a slower speed. If participants missed a turn, the drive ended at that point and then started over from the beginning. The drive ended once participants successfully followed the directions of the drive, i.e., completed four left turns.

Like the second adaptation drive, the third adaptation drive involved completing four right turns at traffic lights or stop signs on two-lane residential roads or two- to four-lane suburban roads. While driving, participants had to turn right when they received the verbal and visual directions from the driving simulator. The research student provided the same cues as in the second adaptation drive for those who experienced difficulty with right turns. The drive ended once participants successfully completed four right turns.

2.3.6.4.5 Main Driving Scenario

After the adaptation drives, participants completed the main driving scenario. Figure 2.2 provides an overview of the scenario, which took approximately 10 minutes to complete when driving between 40 kilometers per hour (25 miles per hour, 11.1 meters per second) and 60 kilometers per hour (37 miles per hour, 16.7 meters per second). The main driving scenario involved maneuvering through 12 straight drives (50%), four left turns (16.5%), three right turns (13%), four hazardous events (16.5%), and one navigational driving task (4%). Each hazardous event and navigational driving task were spaced out to occur about 1.5 minutes apart from one another. Most driving tasks occurred in an urban environment (14 or 58%), followed by suburban (7 or 29%), and then residential environments (3 or 13%).

Description of Main Drive in Driving Simulator Assessment

Administration Instructions: "This drive is about 10 minutes in length. You will travel in residential neighborhoods, a downtown area, and a commercial area with busy intersections. When you need to turn, you will hear the instruction of where to turn and you will see an arrow on the hood pointing in that direction. Throughout the drive, you may have to make decisions to ensure you stay on route towards the city of London. So, you will follow the signs of the road. As in any real-life roadway, you will encounter other vehicles and pedestrians who may or may not follow the rules of the road. If you are uncomfortable or have difficulty during the drive, please let me know. When you are ready you may put the car in drive and begin."

Description of Main Drive
Residential Area
(1) Drive straight at 40 kilometers per hour
(2) Drive straight through traffic light intersection
(3) Turn left at traffic light
Suburban Area
(4) Drive straight
(5) Hazardous event: Car randomly pulls out in front
(6) Drive straight through traffic light intersection
(7) Turn right at traffic light
(8) Drive straight
(9) Hazardous event: Traffic light suddenly changes from green to yellow to red
(10) Turn left at traffic light
City Environment
(11) Drive straight toward downtown at 60 kilometers per hour
(12) Hazardous event: Pedestrian unexpectedly crosses out in front
(13) Turn right at traffic light
(14) Drive straight
(15) Turn left at traffic light
(16) Drive straight
(17) Turn left at traffic light
(18) Hazardous event: Vehicle in front suddenly cross lane in front
(19) Drive straight
(20) Drive straight through traffic light intersection
(21) Drive straight
(22) Turn right at traffic light
(23) Drive straight
(24) Navigational driving task: When driving straight, drivers must scan the environment for the directional road signs to London, Ontario, which indicate to turn right at the next traffic light intersection.

Figure 2.2 Overview of the Main Driving Scenario

2.3.6.4.5.1 Event 1: Car Pulls Out in Front of Drivers

The main driving scenario involved driving in non-inclement weather on a bright sunny day with few clouds. The scenario started in a residential neighborhood with low-rise, one-story properties and progressed to suburban and urban environments with high-rise industrial and commercial properties. Roadways progressed from two-lane roads, with one lane per traveled way, and parking lanes on both shoulders, to four-lane roads, with two lanes per traveled way, and sidewalks on both shoulders.

The order of hazardous events recorded participants' operational driving maneuvers, tactical driving maneuvers, and then a strategic driving maneuver. Event 1 recorded participants' operational driving maneuvers in a suburban environment when responding to a car that suddenly pulled out in front of them (see Figure 2.3). Participants triggered the event to occur by driving over a landmark at the first left turn of the drive (i.e., maneuver 3 in Figure 2.2). After the left turn, participants drove straight about halfway down the road until they approached a stationary car in a parking lane. The event started when the car's left front bumper started to intersect into the driving lane in front of participants. Participants responded by braking or continuing to drive passed the car. The event ended once participants came to a complete stop or drove past the car.

Figure 2.3 Event 1: Car Pulls Out in Front of Drivers by DriveSafety, Inc. (https://drivesafety.com). Adapted with permission.

2.3.6.4.5.2 Event 2: Traffic Light Changes Colours

Event 2 recorded participants' operational driving maneuvers in a suburban environment when responding to a traffic light that suddenly changed from green to yellow and then yellow to red (see Figure 2.4). After event 1, participants drove straight and then made a right turn. After the turn, participants drove straight about halfway down the road until they approached a traffic light intersection. Upon approaching the intersection, the yellow traffic light illuminated (i.e., event start, maneuver 8 in Figure 2.2). Participants responded by braking or continuing to drive through the intersection. The event ended once participants came to a complete stop or drove past the traffic light intersection.

Figure 2.4 Event 2: Traffic Light Changes Colours by DriveSafety, Inc. (https://drivesafety.com). Adapted with permission.

2.3.6.4.5.3 Event 3: Pedestrian Walks in Front of Drivers

Event 3 recorded participants' tactical driving maneuvers in an urban environment when responding to a pedestrian that walked in front of them (see Figure 2.5). After event 2, participants turned left onto an urban road and drove toward a commercial, downtown area. Upon approaching an intersection, the driving simulator directed participants (e.g., verbally and visually) to make a right turn at the intersection (e.g., event trigger). After participants received the directions, they prepared to change lanes (if they were in the left lane) and make a right turn when a pedestrian started to cross the road in front of them (e.g., event start). Participants responded by braking or driving around the pedestrian. The event ended once participants came to a complete stop or drove past the pedestrian.

Figure 2.5 Event 3: Pedestrian Walks in Front of Drivers by DriveSafety, Inc. (https://drivesafety.com). Adapted with permission.

2.3.6.4.5.4 Event 4: Vehicle Cuts Across the Lane in Front of Drivers

Event 4 recorded participants' tactical driving maneuvers in an urban environment when responding to a vehicle that cut across the lane in front of them (see Figure 2.6). After event 3, participants made one right turn and two left turns in the downtown area. After the second left turn, participants approached two stationary vehicles in the left lane. To continue driving, participants had to change into the right lane and pass the stationary vehicles (e.g., event trigger). Once participants were in the right lane, both stationary vehicles started to drive in the left lane. The event started when the slightly ahead vehicle started to intersect into the right lane, crossing in front of participants. Participants responded by braking or driving around the vehicle. The event ended once participants came to a complete stop or drove past the vehicle.

Figure 2.6 Event 4: Vehicle Cuts Across the Lane in Front of Drivers by DriveSafety, Inc. (https://drivesafety.com). Adapted with permission.

2.3.6.4.5.5 Navigational Driving Task

The navigational driving task recorded participants' strategic driving maneuvers in an urban environment (see Figure 2.7). After event 4, participants drove through two traffic light intersections and made one right turn. After the turn, the driving simulator's verbal and visual directions disappeared for the rest of the drive. Participants had to recall the verbal directions the research student provided at the beginning of the drive (e.g., eight to nine minutes prior to the task) to follow the road signs toward London, Ontario, Canada. If participants recalled the verbal directions, they visually searched and scanned the environment to detect road signs that directed them to London, Ontario, Canada. Subsequently, participants initiated turning toward London by signaling right, changing into the right lane if they were originally in the left lane, and making a right turn at the intersection. Accordingly, this navigational driving task required participants to assess the environment, initiate a response, decide on whether to turn left, right, or drive straight through the intersection, and execute their decision.

Figure 2.7 Navigational Driving Task by DriveSafety, Inc. (https://drivesafety.com). Adapted with permission.

2.3.6.4.5.6 Driving Simulator Outcomes

For events 1 to 4 in the main driving scenario, the research student quantified participants adjustment to stimuli maneuvers (operational or tactical) via *reaction time*, *maximum response time*, *mean speed*, and *response type*.

Reaction time indicated the time in seconds from when the event started until the participant's right foot made initial contact with the accelerator or brake pedal (Classen, Dickerson, et al., 2017, p. 24; Society of Automotive Engineers International, 2015, p. 35). Initial pedal contact depended on the location of the right foot when the event started. For example, if participants started with their foot on the accelerator pedal, initial pedal contact was defined as completely releasing the foot off the accelerator pedal. Alternatively, if participants started with their foot on neither pedal, initial pedal contact was defined as initial contact with either accelerator or brake pedal.

Maximum response time indicated the time in seconds from when the event started until the event ended, which depended on whether participants came to a complete stop or drove past the monitor entity (Classen, Dickerson, et al., 2017, p. 24; Society of Automotive Engineers International, 2015, p. 35). The monitor entity referred to the road user or object in each event that interacted with participants, i.e., car in event 1, traffic light in event 2, pedestrian in event 3, and vehicle in event 4.

Mean speed indicated participants' average speed in meters per second from when the event started until it ended (Classen, Dickerson, et al., 2017, p. 24). *Response type* indicated whether participants stopped or failed to stop (e.g., continued to drive).

For the navigational driving task, the research student quantified participants' strategic maneuvers via a *correct decision* vs. *incorrect decision*. A *correct decision* indicated that participants made a right turn toward London, Ontario, Canada. An *incorrect decision* indicated that participants either made a left turn toward Toronto, Ontario, Canada, or drove straight through the intersection.

All measures were verified by DriveSafety™ engineers. These objective simulator kinematic data prevented assessor bias rating the driving performance of study participants.

2.3.6.5 Technology Acceptance Questionnaires

After the driving simulator assessment, participants completed the Perceived Usefulness and Ease of Use Questionnaire (PUEoU; Davis, 1989) and the System Usability Scale (SUS; Brooke & Jordan, 1996) to document their perceptions on the usefulness, usability, and satisfaction of the driving simulator. The PUEoU includes 12 questions about the driving simulator's usefulness and usability. Participants responded to the questions using a seven-point Likert scale, with 1—strongly disagree to 7—strongly agree (Davis, 1989). The SUS includes 10 questions about the driving simulator's usefulness and satisfaction. Participants responded to the questions using a five-point Likert scale, with 1—strongly disagree to 5—strongly agree (Brooke & Jordan, 1996). For the PUEoU and SUS, the research student averaged participants' responses to each question. The research student added these questionnaires into the study protocol to understand whether participants would accept or intend to undergo a driving simulator assessment for their driving performance.

2.3.7 Data Collection and Management

The research student collected, collated, interpreted, and entered all participants' de-identified demographic and medical information, driver behaviour, clinical, and driving simulator outcomes into an SPSS Statistics 26 analysis database (IBM Corporation, 2019); and created a data dictionary that identified the software version and information about the variables, such as name, type, and associated attributes (e.g., code for group). Quality control checks of the data were completed through cross-referencing documentation on testing forms and video-recordings with data in the SPSS database. All hard copy data were stored in a locked room and fireproof locked filing cabinet in the co-investigator's office at the University of Western Ontario or principal investigator's office at the University Hospital. All electronic data were stored on the co-investigator's research drive in the i-Mobile Driving Research Lab or principal investigator's local computer network on a password-protected server as a password protected and encrypted document.

2.3.7.1 Video Recordings

To optimize data collection, the research student used two Logitech C922 Pro Stream cameras to video record the main driving scenario, including participants' eyes and face to observe their movement when maneuvering through the driving scenario and responding to the hazardous events. The cameras recorded high-definition videos with 1080 pixels at 30 frames per second. One camera was located behind the driver to record the simulated drive, while the other camera was located on the simulator's middle monitor screen to record participants' eyes and face. The research student marked locations in the testing room to set up the cameras consistently across participants. The research student connected both cameras to the computer in the driving simulator testing room via two USB extender cables.

During the main driving scenario, the research student used the software "Logitech Capture (https://www.logitech.com/en-ca/product/capture#logitech-pass)" to video record the simulated drive (e.g., entire screen) with participants' eyes and face (e.g., bottom left screen) as one mp4 file. The mp4 video files were stored on a password protected and encrypted folder on the i-Mobile Driving Research Lab's computer drive. Also, the document's name was coded for further confidentiality. The research student viewed each participant's video recordings once to verify data collected on the driving simulator testing form and the metrics collected by the driving simulator. For example, the video recordings verified participants' response type (i.e., stopped vs. failed to stop), occurrence of collisions (i.e., collided vs. did not collide), and the navigational driving task decision (i.e., correct vs. incorrect).

2.3.7.2 Driving Simulator Outcomes

A priori, the research student consulted a civil and coastal transportation research engineer to determine an accurate and feasible method for computing and interpreting the driving simulator data for data analysis. The research student and research engineer agreed upon a method that included the five following steps documented by (Reyes & Lee, 2011, p. 308-323, see Table 2.1). The method was based on consultation with the DriveSafety™ engineer team to understand how the driving simulator collected the data.

Table 2.1 Description of Steps for Computing and Interpreting the Driving Simulator Data

Steps	Description
Step 1: Data access	The data access process involved accessing the data from the driving simulator's computer drive and importing the data into an SPSS database file in the i-Mobile Driving Research Lab. The driving simulator scenarios comprised SimClinic™ software. During the main driving scenario, the SimClinic™ software automatically collected 38 metrics with a frame rate of 60 Hertz for each hazardous event and the navigational driving task. The software automatically saved the collected metrics in a text document on the driving simulator's computer drive. The research student retrieved this text document through WinSCP (https:/winscp.net/eng/index.php), a software program used to transfer files between local and remote computers. Using WinSCP, the research student transferred the text file of each participant's main driving scenario, saved on the driving simulator's computer drive, to the i-Mobile Driving Research Lab's Research drive. Next, the research student imported each participant's data from the main driving scenario, saved as the text file, into an SPSS database file. For 59 participants, the research student imported 59 text files of data from the main driving scenario into 59 SPSS database files.
Step 2: Data reduction	The data reduction process involved writing a code via SPSS syntax to create output of each participant's main driving scenario (saved in the SPSS database file) that included only the data collected during each hazardous event or navigational driving task. The research student's code created output that first organized data by hazardous event or navigational driving task. For each hazardous event or navigational driving task, the code created output that organized the data collected by

Steps	Description
	when the event occurred (vs. before or after the event).
Step 3: Data collection	The data collection process included collecting the metrics needed to measure participants' driving maneuvers (e.g., reaction time, maximum response time, mean speed, response type, occurrence of crashes, navigational driving task decision). During each hazardous event (i.e., from event start to event end), the research student collected the following metrics via creating an output of case (e.g., time at each frame) and summary reports (e.g., means, standard deviations) in the SPSS database. Metrics included the *time* in seconds from the start of the main driving scenario; *accelerator pedal use* from 0% to 100%; *brake pedal use* from 0% to 100%; *mean speed (meters per second)* of the driver's traveling speed during the active event (vs. before and after the event); *time to entity (seconds)*, which indicated the time period for when a collision will occur with the monitor entity (e.g., pedestrian in pedestrian event); and *distance to entity (meters)*, which indicated the straight line distance from the center of the front bumper to the monitor entity (e.g., vehicle in vehicle crosses lane event). For the navigational driving task, the last value in the case summary output indicated participants *correct vs. incorrect decision* for driving toward London, Ontario, Canada, which the research student verified via documentation on the testing form and video recordings.
Step 4: Computing driving performance measures	Computing driving performance measures included manually inspecting the case and summary report output of metrics in each event and navigational driving task, and documenting the metrics needed to compute reaction time, maximum response time, mean speed, response type, simulated collision, and the navigational driving task decision. In an Excel document, the research student documented the following measures using metrics in the output. The *location of the right foot at the start of the event* (e.g., foot is on accelerator) was determined with the first case value in the output for accelerator or brake pedal use. A value >0% would indicate pressing the accelerator or brake pedal. If both values were 0%, the foot was on neither pedal. The *time* when the event started was determined with the first case value in the output for time in seconds from the start of the main driving scenario. This time value would be the denominator when computing reaction time and maximum response time. Participants' *initial response* to the event (e.g., released foot off accelerator) was determined with the accelerator or brake values in the output. For example, if participants started the event with pressing the accelerator (i.e., accelerator value >0%), the initial response would be when they completely released their foot off the accelerator pedal (i.e., accelerator value = 0%). The *time in seconds of the initial response* was determined with the time value for when participants initially responded to the event, such as the time when they completely released their foot off the

Steps	Description
	accelerator pedal. This time value would be the numerator when computing reaction time. The *time in seconds when the event ended* was determined based on whether participants stopped, failed to stop, or demonstrated a collision in response to the event. *For participants who stopped*, the time when the event ended was determined with a speed cut-point ≤.27 meters per second (≤1.0 kilometers per hour, ≤.6 miles per hour). *For participants who failed to stop*, the time when the event ended was determined with the first negative time to entity value in conjunction with a distance to entity value closest to 0.0 meters in response to the event. This time value would be the numerator when computing maximum response time. *For participants who experienced a collision*, the time when the event ended was determined with the collision metric, which documented the name of the monitor entity involved in the collision (e.g., pedestrian in pedestrian event). The time value of this metric would be the numerator when computing maximum response time. For each participant and event, the research student documented the mean and standard deviation of speed in meters per second that was automatically collected by the driving simulator and via syntax code, computed in the case and summary output. *Reaction time* was computed by subtracting the time of the initial response with the time when the event started in seconds (i.e., reaction time = time of initial response / time when event started). *Maximum response time* was computed by subtracting the time when the event ended with the time when the event started in seconds (i.e., maximum response time = time when event ended / time when event started). *Response type* was determined by examining whether the time in seconds when the event ended was determined via a speed value ≤.27 meters per second (≤1.0 kilometers per hour, ≤.6 miles per hour) to indicate a complete stop; the time to entity and distance to entity values to indicate a fail to stop; or whether the collision metric identified the name of a monitor entity to indicate a collision occurred. For the navigational driving task, the driving simulator automatically collected a *correct vs. incorrect decision*, which via coding and running output, was documented in the SPSS case and summary output.
Step 5: Verifying data collection	Verifying data collection involved performing monthly quality checks of the data for each participant through running the case and summary SPSS output of the events and navigational driving task and cross-referencing the output with the metrics and computed driving performance measures in the Excel document. In addition, the research student visually inspected the data through cross-referencing the data in the Excel document with plotted sequence charts of each participant's use of the accelerator and brake pedals, and their speed across time and

Steps	Description
	frame in each event. Response type (i.e., stopped, failed to stop), collision (i.e., collided vs. did not collide), and the navigational driving task decision (i.e., correct vs. incorrect) were verified through documentation on the testing form, which occurred during the driving simulator assessment and via reviewing the video recordings of the main driving scenario.

Note. This method is based on a documented data reduction process by Reyes and Lee (2011, p. 308-323) and via consultation with the DriveSafety™ engineer team of the data collected by the driving simulator for the main driving scenario.

2.3.8 Data Analysis

All data analyses were computed with SPSS Statistics 26 (IBM Corporation, 2019), using two-sided tests with a significance level $\alpha = .05$. Shapiro-Wilk tests of continuous variables indicated that most data were not normally distributed in participants with MS and in participants without MS (see Table 1 in Appendix D, p. 164-169). Computed *z*-scores of continuous data identified one or two outliers (i.e., *z*-score ± 3.3; Warner, 2020, p. 101) in six variables (see Table 2 in Appendix D, p. 164-169). The distribution of continuous data did not change after removing outliers and recomputing Shapiro-Wilk tests (see Table 3 in Appendix D, p. 164-169). Accordingly, Mann-Whitney *U*, Chi-square (x^2), or Fisher's exact tests quantified if differences in demographic characteristics, clinical test scores, or driving simulator performance existed between participants with MS and participants without MS. Spearman rho (r_s) or rank biserial correlations (r_{rb}) quantified the strength and direction of correlational relationships between clinical test scores and driving simulator performance in participants with MS (Portney, 2020, p. 435). Positive or negative correlations <.3 had a weak relationship; .3 to .69 had a moderate relationship; and .7 to 1.0 had a strong to perfect relationship (Jackson, 2009, p. 142).

2.3.8.1 Evaluate Recruitment Capability and Resulting Sample Characteristics

To determine if eligible participants were recruited within the 13-month timeframe, the research student plotted a flow diagram and compared the proposed vs. actual number of individuals who were interested, recruited, and participated in the study. The research student also quantified recruitment sampling methods and the reasons for individuals declining study participation or for study exclusion.

To determine if relevant participants were recruited, the research student quantified between-group differences of demographic and clinical characteristics in participants with MS and participants without MS. As participants were matched by age (i.e., ± 2 years) and sex (i.e., male, female), it was anticipated that neither demographic differed between groups. However, differences in other demographic or clinical characteristics that impact driving performance may have existed.

2.3.8.2 Evaluate Data Collection Procedures and Outcome Measures

To determine the adequacy of the study protocol for participants and how data was completed, the research student quantified the amount of missing data during data collection procedures and examined the reasons for missing data. A cut-point ≥50% missing data indicated to remove variables from analyses (Warner, 2020, p. 143-146).

2.3.8.3 Evaluate the Acceptability and Suitability of the Driving Simulator

2.3.8.3.1 Acceptability

To determine participants' perceptions of the driving simulator's usefulness or usability the research student quantified their responses on the PUEoU and SUS in participants with MS vs. without MS.

2.3.8.3.2 Suitability

To determine whether the onset of SAS affected participants' ability to complete the simulated driving scenarios, the research student calculated the percentage of participants who reported symptoms of SAS (e.g., sweaty, queasy, dizzy, nauseous) on the Modified Motion Sickness Assessment Questionnaire (e.g., baseline, pre-drives, adaptation drives, main drive, post drive), and quantified correlations between reported symptoms of SAS and demographics in those with MS.

2.3.8.4 Evaluate the Resources and Ability to Manage and Implement the Study

To determine if the study had the resources to conduct the study successfully as per the protocol, the research student described the study's resources to conduct the study. The research student also computed the mean time to complete the entire study, which included participant recruitment, informed consent process, screening procedures, intake form, Driver Behaviour Questionnaire, visual and cognitive tests, and driving simulator assessment.

2.3.8.5 Evaluate Preliminary Clinical and Driving Simulator Test Results

To determine whether potential predictive relationships existed between clinical test scores and driving simulator performance in drivers with MS, the research student quantified between-group differences in driving simulator performance between participants with MS and participants without MS. Also, for participants with MS, the research student quantified the strength and direction of bivariate correlations between clinical test scores and driving simulator performance, and considered significant (i.e., $p \leq .05$) correlations between visual or cognitive deficits and driving performance deficits.

2.4 Results

2.4.1 Evaluate Recruitment Capability and Resulting Sample Characteristics

Figure 2.8 presents the number of individuals who expressed interest, enrolled, and participated in the study between January 2019 and February 2020. Overall, 38 individuals with MS (95% of recruitment goal) and 21 individuals without MS (105% of recruitment goal) enrolled and participated in the study. The research student recruited participants with MS via the London MS Clinic (33 or 87%), University mass recruitment email (4 or 11%) or MS Society of Canada's Research Portal (1 or 2%). The research student recruited participants without MS through the University (18 or 86%) or London MS Clinic (3 or 14%).

As displayed in Figure 2.8, most excluded individuals with MS declined participating without providing a reason. Most individuals without MS were excluded because they inquired about the study after recruitment had been completed. The most common reasons for declining study participation were that the study location was too far of a commute or individuals did not have the time to commit to the study. Of those who did not meet the study inclusion criteria, two individuals with MS and two individuals without MS had medical diagnoses that confounded study findings; one individual with MS took medication that confounded study findings; and one individual without MS did not meet the age criterion. Once enrolled in the study, no participants with MS or without MS were excluded.

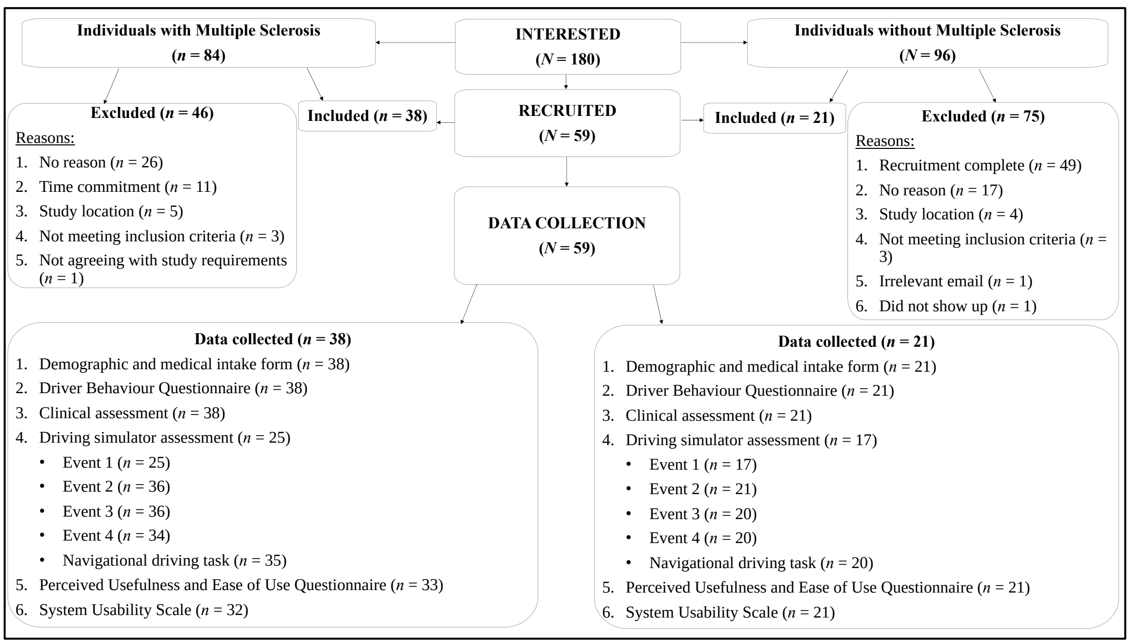

Figure 2.8 Flow Chart of the Number of Individuals with Multiple Sclerosis vs. without Multiple Sclerosis Interested (*N* = 180), Recruited (*N* = 59), Participated and Completed the Study (*N* = 59)

Table 2.2 summarizes demographic and clinical characteristics of participants with MS and participants without MS. Those with MS (vs. without MS) took significantly more medications. No other demographics or clinical tests significantly differed between groups.

In the MS group, 35 participants had relapsing-remitting MS (92%) and three participants had progressive MS (8%). Diagnosis occurred a mean of 10.8 years (*SD* = 9.7 years) prior to the time of the study. As per inclusion criteria, participants had a low level of physical disability (*median* EDSS = 2.0, *IQR* = 1.5), did not experience a relapse three months prior to the time of study (*M* = 3.3 years, *SD* = 3.2), and did not experience severe depression (*M* Beck Depression Index Fast Screen total score = 1.6, *SD* = 2.0) or severe fatigue (Fatigue Severity Scale *M* score = 4.2, *SD* = 1.4).

Table 2.2 Demographic and Clinical Characteristics of Participants with Multiple Sclerosis vs. Participants without Multiple Sclerosis (*N* = 59)

Characteristics	Participants		Between-group difference test
	with MS (*N* = 38)	without MS (*N* = 21)	
Demographic			
Age (years)	42.9 (10.3)	40.0 (9.9)	*U* = 332, *p* =.29
Sex			χ^2 (*df* = 1) = .06, *p* = 1.00
Male	12 (32%)	6 (29%)	
Female	26 (68%)	15 (71%)	
Ethnicity			*Fisher's* = 2.8, *p* = .17
Caucasian	36 (95%)	17 (81%)	
Other	2 (5%)	4 (19%)	
No. medications	3.8 (3.3)	.3 (.6)	*U* = 62.5, *p* <.0001*
No. years education	16.3 (2.8)	17.9 (3.0)	*U* = 277.5, *p* = .053
Employment status			*Fisher's* = .8, *p* = .47
Employed/ Student	31 (82%)	19 (90%)	
Unemployed/ Disabled	7 (18%)	2 (10%)	
No. years driving	25.2 (10.8)	23.7 (10.7)	*U* = 366, *p* = .61
No. days driven/ week	6.0 (1.8)	5.5 (2.5)	*U* = 374, *p* = .65
No. kilometers driven/ day	43.0 (44.6)	30.2 (37.3)	*U* = 315.5, *p* = .19
Professional driver			*Fisher's* = 2.2, *p* = .24
Yes	7 (18%)	1 (5%)	
No	31 (82%)	20 (95%)	
Clinical Test Scores			
DBQ (*M* score, 1-6)			
Slips	1.6 (.3)	1.7 (.3)	*U* = 312.0, *p* = .17
Violations	1.4 (.3)	1.6 (.4)	*U* = 336.0, *p* = .32
Mistakes	1.7 (.4)	1.7 (.4)	*U* = 359.5, *p* = .54
Visual acuity			*Fisher's* = 1.0, *p* = .41
≤20/40	33 (87%)	20 (95%)	
≥20/50	5 (13%)	1 (5%)	
Useful Field of View™ (milliseconds)			

Characteristics	Participants		Between-group difference test
	with MS (N = 38)	without MS (N = 21)	
Subtest 1	17.9 (3.6)	17.3 (3.4)	U = 344.5, p = .39
Subtest 2	35.0 (60.7)	20.0 (4.8)	U = 339.0, p = .35
Subtest 3	62.3 (79.1)	46.7 (37.4)	U = 369.0, p = .64
SDMT (/90s)	58.8 (12.3)	65.5 (11.5)	U = 287.5, p = .08
CVLT2-IR (/80)	56.3 (10.8)	58.9 (10.0)	U = 369.5, p = .65
BVMTR-IR (/36)	26.1 (7.1)	26.8 (6.1)	U = 391.5, p = .91
BVMTR-DR (/12)	9.7 (2.4)	10.2 (2.4)	U = 331.0, p = .27

Note. Summary statistics: continuous data = means (standard deviations); categorical data = frequencies (percentages).
MS = Multiple Sclerosis; DBQ = Driver Behaviour Questionnaire; SDMT = Symbol Digit Modalities Test-Oral Version; CVLT2 = California Verbal Learning Test-Second Edition; IR = Immediate Recall; DR = Delayed Recall; BVMTR = Brief Visuospatial Memory Test-Revised Version.
*$p \leq .05$, two-tailed.

2.4.2 Evaluate Data Collection Procedures and Outcome Measures

Up to seventeen (28.8%) participants had missing data in the driving simulator assessment. During the first left turn of the main driving scenario, eleven participants with MS and four participants without MS drove over the sidewalk and missed the landmark to trigger event 1 to occur. Accordingly, those participants had missing data for event 1. One participant with MS (reported before event 1) and one participant without MS (reported after event 2) reported symptoms of SAS, which resulted in missing data for the remaining of the drive. One participant with MS had missing data for the entire driving assessment because the driving simulator did not load any of the pre-driving, adaptation, or main driving scenarios. Two participants with MS had missing data for event 4 as the event did not occur in their drive. Lastly, during event 4, one participant with MS experienced a collision and the scenario would not advance any further, resulting in missing data for the navigational driving task.

Five participants with MS did not complete the PUEoU and SUS because they completed the study before the research student added the questionnaires to the study protocol. Furthermore, one participant with MS did not complete the SUS during the study visit. When testing the five participants, the research student observed different driving performance responses to events (e.g., stopped, failed to stop, collision), including the onset of SAS. Accordingly, the research student added the PUEoU and SUS into the study protocol to examine whether demographic (e.g., age, sex), clinical (e.g., losses in visual and cognitive ability), and/or driving characteristics (e.g., SAS) affected participants' intention to use a driving simulator.

2.4.3 Evaluate the Acceptability and Suitability of the Driving Simulator

Table 2.3 presents both group's mean responses on the PUEoU and SUS regarding the usefulness, usability, and satisfaction of the driving simulator. Mean responses on both questionnaires did not significantly differ between groups. On the PUEoU, participants' *mean* responses varied from slightly disagree (item rating = 3) to slightly agree (item rating = 5). On the SUS, participants' *mean* responses varied from strongly disagree (item rating = 1) to agree (item rating = 4).

Table 2.3 Participants' Mean Responses on the Perceived Usefulness and Ease of Use Questionnaire (*N* = 54) and System Usability Scale (*N* = 53)

Questionnaire Statement	Participants				Mann-Whitney *U* test	
	with MS		without MS			
	M	*SD*	*M*	*SD*	*value*	*p*
Perceived Usefulness and Ease of Use						
1. Using a driving simulator would enable me to accomplish driving tasks more effectively	3.5	1.7	3.8	1.8	318.5	.62
2. Using a driving simulator would improve my driving performance	3.4	1.7	3.5	1.7	331.0	.79
3. Using a driving simulator would increase my driving skills	3.6	1.7	3.2	1.6	309.5	.51
4. Using a driving simulator would enhance my effectiveness in driving	3.8	1.6	3.4	1.7	301.0	.42
5. Using a driving simulator would make it easier to drive	3.2	1.6	3.2	1.8	345.0	.98
6. I would find a driving simulator to be useful for my driving	3.2	1.5	3.1	1.6	321.0	.65
7. Learning to operate a driving simulator would be easy for me	4.4	1.6	4.7	1.6	312.0	.54
8. I would find it easy to get a driving simulator to do what I want it to do	3.7	1.6	4.2	1.6	284.0	.26
9. My interaction with a driving simulator would be clear and understandable	4.9	1.6	5.0	1.3	337.0	.87
10. I would find a driving simulator flexible	4.6	1.5	4.5	1.2	307.0	.48

Questionnaire Statement	Participants				Mann-Whitney *U* test	
	with MS		without MS			
	M	*SD*	*M*	*SD*	*value*	*p*
to interact with						
11. It would be easy for me to become skillful at using a driving simulator	4.7	1.5	5.1	1.2	296.0	.36
12. I would find a driving simulator easy to use	4.9	1.6	4.8	1.4	327.0	.73
System Usability Scale						
1. I think that I would like to use this system frequently	2.2	.9	2.2	1.1	330.5	.94
2. I found the system unnecessarily complex	1.6	.7	1.7	.8	323.5	.84
3. I thought the system was easy to use	3.8	1.3	3.9	1.0	321.5	.79
4. I think that I would need the support of a technical person to be able to use this system	2.5	1.4	2.0	1.3	271.0	.23
5. I found the various functions in this system were well integrated	3.8	1.0	3.5	.9	273.5	.24
6. I thought that there was too much inconsistency in this system	2.3	1.1	2.1	1.0	308.5	.61
7. I would imagine that most people would learn to use this system very quickly	3.6	1.2	3.6	.8	313.0	.67
8. I found the system to be very cumbersome to use	2.3	1.0	2.4	.9	301.5	.51
9. I felt very confident using the system	3.3	1.2	3.5	1.0	306.0	.58
10. I needed to learn a lot of things before I could get going with this system	2.0	1.1	2.0	1.0	329.0	.90

Note. Perceived Usefulness and Ease of Use Questionnaire: Number of participants included in analysis = 33 participants with MS; 21 participants without MS. Item ratings include: 1 = strongly disagree; 2 = moderately disagree; 3 = slightly disagree; 4 = neutral; 5 = slightly agree; 6 = moderately agree; 7 = strongly agree.
System Usability Scale: Number of participants included in analysis = 32 participants with MS; 21 participants without MS. Item ratings include: 1 = strongly disagree; 2 = disagree; 3 = neutral; 4 = agree; 5 = strongly agree.

Seven (19%) participants with MS and two (10%) participants without MS experienced the onset of SAS. As displayed in Table 2.4, participants reported symptoms of SAS during or after the main driving scenario.

Table 2.4 Participants' Reported Symptoms of Simulator Adaptation Syndrome during the Driving Simulator Assessment (*N* = 58)

Time of Rating	Frequencies and Percentages of Reported Symptoms of Simulator Adaptation Syndrome			
	Sweaty	Queasy	Dizzy	Nauseous
Baseline	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pre-drive 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Pre-drive 2	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adaptation drive 1	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adaptation drive 2	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Adaptation drive 3	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Main driving scenario	1 (2%)	4 (7%)	5 (9%)	3 (5%)

Note. Reported ratings ranged from 0—not at all, to 10—severely on the Modified Motion Sickness Assessment Questionnaire.

Table 2.5 presents the bivariate correlations between demographic characteristics and reported symptoms of SAS in participants with MS. Bivariate correlations showed that female (vs. male) sex, greater fatigue (Fatigue Severity Scale), reporting more years since last relapse, and reporting more medications moderately correlated with reporting increased symptoms of dizziness.

Table 2.5 Bivariate Correlations of Demographic Characteristics and Reported Symptoms of Simulator Adaptation Syndrome in Participants with Multiple Sclerosis (*N* = 37)

Demographic Characteristics	Reported Symptoms of Simulator Adaptation Syndrome			
	Sweaty	Queasy	Dizzy	Nauseous
Age (years) [a]	.2	−.0	.3	−.1
Sex (male = 1, female = 2) [b]	.2	.2	.4*	.1
BDIFS (*M* Total score, 0-21) [a]	.3	.1	.2	−.2
FSS (*M* score) [a]	.3	−.1	.4*	−.0
MS Diagnosis (RRMS = 1, Progressive MS = 2) [b]	.2	.0	−.1	−.1
Years since MS diagnosis [a]	.1	−.1	.0	−.2
Years since last relapse [a]	−.1	.1	.3*	−.2
No. medications [a]	.3	.1	.4*	−.0

Note. Reported ratings ranged from 0—not at all, to 10—severely on the Modified Motion Sickness Assessment Questionnaire during or after the main driving scenario. BDIFS = Beck Depression Index-Fast Screen; FSS = Fatigue Severity Scale; MS = Multiple Sclerosis; RRMS = Relapsing-remitting Multiple Sclerosis.

[a]Spearman rho correlation; [b]Rank biserial correlation.

*$p \leq .05$, two-tailed.

2.4.4 Evaluate the Resources and Ability to Manage and Implement the Study

This study had no external funding and the supervisory team covered all fees (e.g., University poster distribution services, participant compensation) through undesignated funds, and cost-share of faculty time. Further, with support from the supervisory team, the research student obtained all screening and assessment administration manuals, assessment forms, software, and equipment needed to conduct the study. Notably, the principal and co-principal investigators oversaw all aspects of the study from conception to dissemination. The co-investigator supplied testing and infrastructure support in the i-Mobile Driving Research Lab, which included access to testing and observation rooms, and testing equipment (i.e., OPTEC® 5000 Peripheral-Glare Vision Screener, UFOV, driving simulator), forms, and manuals. The research coordinator assisted with daily administrative tasks, and participant recruitment, screening, and informed consent procedures. The research student completed daily administrative tasks, participant recruitment, screening, informed consent, testing procedures, data management and analysis, interpretation, manuscript writing, and research dissemination.

Recruiting participants involved setting up collaborations with the London MS Clinic, MS Society of Canada, and Lawson's Health Research Institute. Other recruitment methods involved using the University's poster distribution services for eight months to post recruitment advertisements around campus for a fee of $170 CAD, and monthly requests to post recruitment advertisements via online networks (i.e., Kijiji, Craigslist, local newspapers).

Overall, each participant took a *mean* of 122 minutes (*SD* = 24.0) to complete the entire study. The informed consent process occurred at the beginning of study visits. Prior to screening and testing procedures, the research student obtained participants' written informed consent, which took about 15 minutes. During this process, only one individual with MS declined study enrolment, as displayed in Figure 2.8 (p. 59). Screening procedures took about 20 minutes and did not result in excluding any participant for not meeting the study's inclusion or exclusion criteria. Clinical testing took about 60 minutes to complete. The Driver Behaviour Questionnaire took the longest (about 10 minutes) for participants to complete. The SDMT, CVLT2-IR, BVMTR-IR, and BVMTR-DR took the longest to administer (about 40 minutes). The driving simulator assessment took about 30 minutes to complete, and as previously discussed in "Evaluate Data Collection Procedures and Outcome Measures," resulted in the most values with missing data (p. 61).

After data collection, the research student scored and entered all data into the SPSS database, which took about 60 minutes to complete per participant. The monthly quality checks of driving performance measures took about 10 minutes per participant. The method for computing participants' driving outcomes involved collaborating with a civil and coastal transportation research engineer. Statistical analysis involved collaborating with a statistician, who provided service free of charge. Report writing and dissemination of study findings will involve preparing and submitting manuscripts in rehabilitation, MS, or transportation journals, and via scientific conference presentations.

2.4.5 Evaluate Preliminary Clinical and Driving Simulator Test Results

2.4.5.1 Between-Group Differences

Table 2.6 summarizes the driving simulator outcomes of the main driving scenario in participants with MS vs. participants without MS. When comparing groups, participants with MS had a significantly slower maximum response time (seconds) when the pedestrian walked across the road in front of them, and more participants with MS crashed when the vehicle crossed lanes in front of them.

Table 2.6 Driving Simulator Outcomes of Participants with Multiple Sclerosis vs. Participants without Multiple Sclerosis (*N* = 59)

Driving Simulator Outcomes	Participants		Between-group difference test
	with MS (*N* = 38)	without MS (*N* = 21)	
Event 1: Car Pulls Out in Front of Drivers			
Reaction time	1.3 (.4)	1.3 (.5)	$U = 208.5$, $p = .92$
Maximum response time	3.8 (.7)	3.6 (.6)	$U = 187.5$, $p = .53$
Mean speed	8.2 (1.7)	8.6 (1.2)	$U = 190.0$, $p = .58$

Driving Simulator Outcomes	Participants with MS (N = 38)	Participants without MS (N = 21)	Between-group difference test
Event 2: Traffic Light Changes Colours			
Reaction time	1.0 (.6)	1.0 (.6)	U = 342.5, p = .56
Maximum response time	2.2 (.4)	2.3 (.4)	U = 289.5, p = .15
Mean speed	11.6 (2.6)	10.9 (3.1)	U = 312.0, p = .28
Response type			χ^2 (df = 1) = 3.6, p = .10
Stopped	13 (36%)	13 (62%)	
Failed to stop	23 (64%)	8 (38%)	
Event 3: Pedestrian Walks in Front of Drivers			
Reaction time	1.3 (.6)	1.4 (.6)	U = 342.0, p = .76
Maximum response time	3.9 (.7)	3.5 (.5)	U = 220.0, p = .02*
Mean speed	7.2 (2.8)	6.8 (2.4)	U = 322.0, p = .53
Response type			*Fisher's* = .5, p = .70
Stopped	30 (83%)	18 (90%)	
Failed to stop	6 (17%)	2 (10%)	
Event 4: Vehicle Cut Across Lane in Front of Drivers			
Reaction time	.9 (.4)	.9 (.5)	U = 296.0, p = .44
Maximum response time	2.5 (1.2)	2.6 (1.5)	U = 328.0, p = .84
Mean speed	8.1 (2.2)	8.6 (3.5)	U = 318.0, p = .70
Response type			*Cramer's V* = .3, p = .04*
Stopped	19 (56%)	14 (70%)	
Failed to stop	2 (6%)	4 (20%)	
Crashed	13 (38%)	2 (10%)	
Navigational Driving Task Decision			*Fisher's* = .0, p = 1.00
Correct	28 (80%)	16 (80%)	
Incorrect	7 (20%)	4 (20%)	

Note. Summary statistics: continuous data = means (standard deviations); categorical data = frequencies (percentages).
Number of participants included in analysis: Event 1 = 25 participants with MS, 17 participants without MS; Event 2 = 36 participants with MS, 21 participants without MS; Event 3 = 36 participants with MS, 20 participant without MS; Event 4 = 34 participants with MS, 20 participant without MS; Navigational Driving Task = 35 participants with MS, 20 participant without MS.
Reaction time is measured in seconds; Maximum response time is measured in seconds; Mean speed is measured in meters per second.
MS = Multiple Sclerosis.
*$p \leq .05$, two-tailed.

2.4.5.2 Bivariate Correlations

Table 2.7 presents the bivariate correlations between clinical test scores and driving simulator performance in participants with MS. In the traffic light event, deficits in immediate verbal/auditory recall (CVLT2-IR), divided attention (UFOV2), and selective attention (UFOV3) moderately correlated with slower maximum response time (seconds) or slower mean speed (meters per second). In the pedestrian event, deficits in immediate verbal/auditory recall (CVLT2-IR) moderately correlated with slower reaction time (seconds). In the navigational driving task, slower selective attention (UFOV3) moderately correlated with incorrect (vs. correct) decisions.

Participants' selective attention (UFOV3) correlated with divided attention (UFOV2; r_s = .6, p <.0001) and immediate verbal/auditory recall (CVLT2-IR; r_s = –.5, p = .003). As immediate verbal/auditory recall (CVLT2-IR) and divided attention (UFOV2) did not correlate with one another (r_s = –.2, p = .29), the research student included both clinical tests to quantify their predictive relationship with driving simulator performance in drivers with MS, as compared to drivers without MS.

Table 2.7 Bivariate Correlations Between the Clinical Test Scores and Driving Simulator Performance of Participants with Multiple Sclerosis (*N* = 38)

Driving Simulator Outcomes	Clinical Test Scores							
	Visual acuity (<20/40 vs. ≥20/50)	UFOV (milliseconds)			SDMT (/90s)	CVLT2 IR (/80)	BVMTR	
		1	2	3			IR (/36)	DR (/12)
Event 1: Car Pulls Out in Front of Drivers								
Reaction time[a]	–.2	–.1	–.2	–.2	.1	–.1	.2	.2
Maximum response time[a]	–.1	–.3	–.0	–.2	–.0	.0	.1	.1
Mean speed[a]	.1	.0	.3	–.0	.1	.1	.2	.2
Event 2: Traffic Light Changes Colours								
Reaction time[a]	.0	–.2	–.2	–.2	.1	.1	.1	–.0
Maximum response time[a]	.0	.2	.4*	.2	–.1	–.2	–.1	.0
Mean speed[a]	–.0	–.2	–.2	–.4*	.1	.4*	.1	.0
Response type[b]	–.1	–.2	–.3	–.2	.1	.2	.1	.0
Event 3: Pedestrian Walks in Front of Drivers								
Reaction time[a]	–.1	–.0	.1	.2	–.2	–.4*	–.3	–.3
Maximum response time[a]	–.1	–.0	.2	–.1	.2	–.1	.2	.1
Mean speed[a]	.2	–.2	.0	–.0	.2	–.2	.2	.2
Response type[b]	.1	–.1	–.0	.0	.1	–.2	.1	.1
Event 4: Vehicle Cut Across Lane in Front of Drivers								

Driving Simulator Outcomes	Clinical Test Scores							
	Visual acuity (<20/40 vs. ≥20/50)	UFOV (milliseconds) 1	2	3	SDMT (/90s)	CVLT2 IR (/80)	BVMTR IR (/36)	DR (/12)
Reaction time[a]	.1	–.2	–.0	–.3	.2	–.1	.1	.2
Maximum response time[a]	–.2	.0	.2	–.0	–.2	–.3	–.3	–.2
Mean speed[a]	.3	–.1	.2	.2	.0	–.2	.0	–.1
Response type[b]	.2	–.1	–.1	.1	.1	.2	.2	.1
Navigational Driving Task								
Decision[b]	–.2	–.1	.2	.4*	–.3	–.3	–.3	–.3

Note. Number of participants with MS included in analysis: Event 1 = 25; Event 2 = 36; Event 3 = 36; Event 4 = 34; Navigational Driving Task = 35.
Reaction time is measured in seconds; Maximum response time is measured in seconds; Mean speed is measured in meters per second; Response type is dichotomized as stopped vs. failed to stop, except in event 4 where it is categorized as stopped vs. failed to stop vs. crashed; Decision is dichotomized as correct vs. incorrect.
UFOV = Useful Field of View™; 1 = UFOV Subtest 1; 2 = UFOV Subtest 2; 3 = UFOV Subtest 3; CVLT2 = California Verbal Learning Test-Second Edition; BVMTR = Brief Visuospatial Memory Test-Revised Version; IR = Immediate Recall; DR = Delayed Recall.
[a]Spearman rho correlations; [b]Rank biserial correlations.
*$p \leq .05$, two-tailed.

2.5 Discussion

Through a feasibility framework (Orsmond & Cohn, 2015), this study examined the feasibility of utilizing visual and cognitive clinical tests to indicate driving simulator performance in drivers with MS, when compared to drivers without MS. Feasibility was examined via evaluating: 1) Recruitment capability and resulting sample characteristics; 2) Data collection procedures and outcome measures; 3) The acceptability and suitability of the driving simulator; 4) The resources and ability to manage and implement the study; and 5) Preliminary clinical and driving simulator test results.

2.5.1 Evaluate Recruitment Capability and Resulting Sample Characteristics

Though twice as many individuals expressed interest in the study, the research student did not reach the goal to recruit 40 participants with MS within the timeframe. Instead, two to three (vs. four) participants with MS were recruited per month. Conversely, the goal for recruiting 20 participants without MS was achieved. Based on these findings, meeting the proposed sample size of 40 participants with MS and 20 participants without MS, would require interest from at least two to three times as many individuals and would take between 13 and 20 months to complete. To ensure feasible planning and realistic timelines for MS driving studies, future researchers may adjust study recruitment expectations according to these study findings.

Consistent with on-road studies and driving simulator studies for individuals with MS, the research team recruited most participants with MS (87%) through an MS Clinic that treated or assessed patients (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Classen et al., 2018; Devos et al., 2017; Kotterba et al., 2003; Krasniuk et al., 2017; Lamargue-Hamel et al., 2015; Raphail et al., 2020). Likewise, most participants without MS (86%) were recruited through the infrastructure and networks of the first author's affiliation (i.e., university; Classen et al., 2018; Kotterba et al., 2003; Lamargue-Hamel et al., 2015). As such, participants with MS may over-represent those involved in a tertiary care center; and participants without MS may over-represent the graduate student population.

In this study, participants with MS showed some differences in clinical characteristics when compared to the population-based sample of those with MS. For example, 92% of participants (vs. 85% of the MS population) had relapsing-remitting MS, while 8% of participants (vs. 15% of the MS population) had progressive MS (Public Health Agency of Canada, 2018). Consistent with other driving studies, most demographic (e.g., age, sex, years education) and clinical characteristics did not significantly differ between participants with MS and without MS (Classen et al., 2018; Devos et al., 2013; Lamargue-Hamel et al., 2015; Marcotte et al., 2008). Overall, these study findings demonstrated that the research student implemented feasible recruitment methods. Though a greater percentage of participants had relapsing-remitting MS (vs. progressive MS) when compared to the MS population and some driving studies, and demographic characteristics such as age, sex, and years of education, did not significantly differ between groups, these findings coincided with the MS literature on driving. The differences in demographic and clinical characteristics might have been mitigated if the research team recruited more participants through the community (e.g., community halls, health facilities) in addition to institutions where they are assessed or treated. As such, the research student continues to suggest using a variety of recruitment strategies, in addition to recruiting through institutions that assess or treat individuals with MS.

2.5.2 Evaluate Data Collection Procedures and Outcome Measures

Participants in this study had missing data during the driving simulator assessment; mostly in event 1 when the car pulled out in front of drivers. Missing data might have been mitigated via pilot-testing the driving scenario multiple times prior to data collection. Such testing could have involved making driving errors on purpose, such as driving over the sidewalk instead of the road, to ensure that the driving simulator collected metrics in all driving scenarios. Furthermore, collaborating with simulator engineers about the process of triggering hazardous events to start might have minimized the number of bypassed events. However, such consultations are costly, especially given that the study had no external funding to offset the cost of specialty consultations. Based on the experience in this study, four strategies include the following: 1) Pilot test the drives and driving performance measures to ensure proper functioning and data collection of the simulator; 2) Ensure that computer programming occurs as to "hit" the landmark that cues hazardous events to start; 3) Video record driving scenarios to supplement failure of the driving simulator to record such data; and 4) Include additional practice drives with turns so that participants become more accustomed to turning; especially due to the 55-degree (vs. 110-degree) field of view on this simulator.

2.5.3 Evaluate the Acceptability and Suitability of the Driving Simulator

Participants' mean responses on the PUEoU (e.g., slightly disagree to slightly agree) and SUS (e.g., strongly disagree to agree) varied in those with MS and without MS. The research student is not sure whether some responses resulted from poor physical and/or psychological fidelity, the task difficulty, and/or some participants experiencing symptoms of SAS. Researchers may want to consider these issues as they plan driving simulator studies for people with MS.

To the research student's knowledge, this is the second study to report the onset of driving SAS in drivers with MS. In the prior driving simulator study, 14% (6/ 42) of participants with relapsing-remitting MS experienced symptoms of SAS (Akinwuntan et al., 2014). Likewise, in this study, findings showed 19% of participants with MS to have SAS. Most reported symptoms of queasiness, dizziness, and/or nausea. Correlations showed that female (vs. male) sex, greater fatigue (Fatigue Severity Scale), reporting more years since last relapse, and reporting taking more medications may contribute to increased symptoms of SAS. Given the vestibular impairment common to the MS population (Akinwuntan et al., 2014; Dunlap et al., 2019; Kasser & Jacobs, 2014), the research student anticipated the onset of SAS to be higher in those with MS than without MS. However, researchers may want to consider empirical testing of the physiological mechanisms underlying the onset of SAS in people with MS. Further, researchers may also need to consider implementing rigorous mitigation protocols to reduce or prevent SAS, and to report results of the onset of SAS. Therefore, these findings demonstrate that a driving simulator may be suitable for drivers with MS, but some may experience symptoms of SAS that affect their ability to drive a simulator.

2.5.4 Evaluate the Resources and Ability to Manage and Implement the Study

Though the available resources enabled the research team to conduct the study, some were not optimal for detecting underlying impairments of driving performance of drivers with MS. For instance, during the main driving scenario, the navigational driving task did not adequately assess participants' strategic driving maneuvers, which depends on high-level reasoning, planning, judging, or problem-solving. Optimizing the navigational driving task would have required an added expense, and as such, the team chose to use an existing driving scenario with a strategic maneuver component—but not to the extent required to make a targeted assessment.

As discussed in "Evaluate the Resources and Ability to Manage and Implement the Study" (p. 65), a considerable amount of time, planning, and management went into conducting the study. For example, for each participant, collecting (i.e., M = 122 minutes, SD = 24.0) and then scoring, computing, and entering data into the statistical database (i.e., about 60 minutes to complete) totaled to about 3.0 hours (182 minutes). For all 59 participants, this time totaled to 179 hours (10,738 minutes). Overall, the proposed number of research team members matched the actual number of research team members required to conduct the study. However, as the team did not completely reach their participant recruitment goal (95% complete), future studies may consider adding more research team members for active recruitment.

Establishing collaborations with the London MS Clinic and MS Society of Canada was successful, as the research team recruited participants through these organizations. As some individuals declined enrolling and participating due to the study's time commitment, reducing the time may improve recruitment rates. For example, future studies may consider asking participants to complete the intake form and Driver Behaviour Questionnaire prior to pursuing the actual clinical component of the study. However, reducing time through this process may reduce the rigour or control of data collection procedures. Therefore, with supervisory, consultative, and community support, the research student had feasible resources to implement the study, and provided suggestions that may enhance the feasibility of future studies.

2.5.5 Evaluate Preliminary Clinical and Driving Simulator Test Results

Preliminary test results showed that tactical maneuvers differed between drivers with MS and without MS. Notably, the slower maximum response time showed that drivers with MS took longer to completely stop or drive past the pedestrian that walked out in front of them. Also, the higher number of drivers with MS to experience a collision indicated that they failed to respond in a timely manner to the vehicle that cut across the lane in front. Both events required drivers to visually search and scan, process, attend to, judge, decide, and respond to critical roadway information. Accordingly, these findings suggest that tactical maneuvers, such as those involved in the pedestrian and vehicle crosses lane events, may target driving performance deficits in drivers with MS.

The bivariate correlations for drivers with MS showed that deficits in immediate verbal/auditory recall (CVLT2-IR), slower divided attention (UFOV2), and slower selective attention (UFOV3) may indicate driving performance deficits in operational, tactical, or strategic driving maneuvers. These findings indicate that drivers with deficits in immediate verbal/auditory recall may take longer to recall, or may not recall, the prior verbal/auditory information. For example, the verbal instructions at the beginning of the drive stated that pedestrians and other road users may or may not follow the rules of the road. During the pedestrian event, drivers who had difficulty recalling the verbal instructions took longer to respond to the pedestrian walking out in front of them, and as such had slower mean speed or slower response time. Furthermore, drivers with difficulty in divided attention or selective attention may take longer to visually search and scan, detect, judge, assess, and respond to critical roadway information while ignoring competing information, and as such, have slower mean speed or response time.

Overall, these study findings suggest that the UFOV2, UFOV3, or CVLT2-IR may underlie driving performance impairments, measured through deficits in operational, tactical, and/or strategic driving maneuvers of drivers with MS. Based on the significant findings, the research student determined that quantifying the predictions would be feasible. Since the UFOV3 correlated with the UFOV2 and CVLT2-IR, the research student considered the UFOV2 and CVLT2-IR as predictors of driving performance. Quantifying the predictive relationships between these clinical tests and deficits in operational, tactical, and/or strategic maneuvers would validate whether the clinical tests and/or driving simulator assessment target driving performance impairment in drivers with MS. As such, the research student considered the UFOV2 and CVLT2-IR to examine their predictive relationships with driving simulator performance measures, with a larger, complete sample (N = 60).

2.5.6 Limitations

Study findings may only be generalized to individuals who meet the sample's characteristics for individuals with MS and without MS. All participants voluntarily enrolled in the study and knew about the neurologist's responsibility to report drivers with conditions that made driving dangerous to the Ministry of Transportation of Ontario, Thus, selection bias may be evident. Most participants with MS were women, 30 to 50 years old, with relapsing-remitting MS and low physical disability, from one tertiary MS

Clinic (87%), while most participants without MS over-represented one university (86%). Thus, spectrum bias may be evident.

This study included a pre-existing driving scenario that was developed, refined, and validated to identify adjustment to stimuli and visual scanning errors of youth drivers (Alvarez et al., 2019; Alvarez, Classen, Medhizadah, Knott, Asantey, et al., 2018; Alvarez, Classen, Medhizadah, Knott, & He, 2018). As such, the main driving scenario did not detect gap acceptance errors, which also indicate decreased on-road outcomes in drivers with MS (Classen, Krasniuk, et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2017). Further, the navigational driving task did not adequately detect strategic driving maneuvers for drivers with MS.

2.5.7 Strengths

Supervisory and consultative teams consisted of multidisciplinary professionals with expertise in driver rehabilitation science, biostatistics, MS, neurology, occupational therapy, driving simulation, and transportation engineering. The team members' shared costs, time, and resources enabled the research student to conduct the study. Inclusion and exclusion criteria ensured that participants met the Ministry of Transportation of Ontario's standards to drive legally (e.g., valid driver's license, vision standards). Though the research student knew participants' diagnoses and clinical test scores, the kinematic data obtained on the driving simulator was objective. Furthermore, video-recording the main scenario and documenting driving outcomes on the standardized assessment form enabled the research student to cross-reference metrics obtained by the driving simulator and those observed from the drive.

The findings in this study contribute to understanding the feasibility of utilizing clinical tests to indicate driving simulator performance in drivers with MS. Notably, findings provided insight to the recruitment rates, data collection procedures, resources, management, and timeframe needed to implement the study. Perceptions of acceptability toward the driving simulator were reported. Further, findings identified some issues that could occur with using driving simulators, such as missing data or the onset of SAS. Overall, the findings in this study provided the foundation for determining clinical predictions of driving simulator performance in drivers with MS. The research student provided suggestions for future studies accordingly—that when considered, may enhance the rigor, time, data collection procedures, and outcomes of future studies.

2.6 Conclusion

This study examined the feasibility of conducting research to understand if clinical tests can predict driving simulator performance in drivers with MS, when compared to drivers without MS. Overall, study findings indicated that it would be feasible to execute a full-scale study; however, findings also highlighted the challenges that exist with conducting driving research for drivers with MS. Notably, the lower than proposed recruitment rates of drivers with MS highlighted the importance of ensuring feasible planning, realistic timelines, and using a variety of recruitment methods to reach recruitment and enhance the generalizability of study findings to the MS population. The missing data on the driving simulator emphasized the importance of understanding the data collection and outcome measures, often automatically collected by the driving simulator. Participants' varied responses toward the usefulness and usability brought novel insight to their perceptions of using a driving simulator for their driving performance. The suitability of the driving simulator showed that some drivers experience symptoms of SAS that will affect their ability to complete the scenarios. With supervisory, consultative, and community support, the research student had the resources to implement the study. Lastly, preliminary test results identified that immediate verbal/auditory recall (CVLT2-IR) and divided attention (UFOV2) may underlie driving performance deficits on a driving simulator. If clinical tests predict driving performance deficits, they may be useful for validating decisions about driving performance in drivers with MS.

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Chapter 3

3 Clinical Predictors of Driving Simulator Performance in Drivers with Multiple Sclerosis

In the prior feasibility study (see Chapter 2, p. 34-82), study findings confirmed the feasibility of utilizing clinical tests (i.e., CVLT2-IR, UFOV2) to assess and indicate driving simulator performance in drivers with MS. Specifically, drivers with MS took longer than drivers without MS to completely stop or pass the pedestrian that walked out in front of them (*M* maximum response time: participants with MS = 3.9 seconds, *SD* = .7 vs. participants without MS = 3.5 seconds, *SD* = .5, *U* = 220.0, *p* = .02). Further, deficits in immediate verbal/auditory recall (CVLT2-IR) and slower divided attention (UFOV2) moderately correlated with adjustment to stimuli errors (operational or tactical) or strategic recall errors in the simulated drive (see Chapter 2, p. 67-69). These findings suggest that tactical adjustment to stimuli errors may underlie driving performance impairment in drivers with MS, when compared to those without MS. Further, deficits in immediate verbal/auditory recall and in divided attention may contribute to driving performance impairment in drivers with MS. Therefore, based on the prior feasibility study findings, this study will examine if the CVLT2-IR and/or UFOV2 can predict driving simulator performance in drivers with MS. If clinical tests can predict driving simulator performance, they may be useful for screening driving performance impairments in drivers with MS.

3.1 Objective

This study will examine if clinical tests (i.e., CVLT2-IR, UFOV2) can indicate driving simulator performance deficits in drivers with MS.

3.2 Aim

This study will quantify if deficits in immediate verbal/auditory recall (CVLT2-IR) and/or slower divided attention (UFOV2) can predict adjustment to stimuli errors (operational and/or tactical) and/or strategic recall errors on a driving simulator in drivers with MS, as compared to control drivers without MS.

3.3 Hypothesis

Based on preliminary test results (see Chapter 2, p. 66-69), it is hypothesized that at least one clinical test (i.e., CVLT2-IR, UFOV2) will predict adjustment to stimuli errors (operational and/or tactical) and/or strategic recall errors in drivers with MS (vs. drivers without MS).

3.4 Methods

This study includes the same methods and procedures as documented in the prior feasibility study (see Chapter 2, p. 36-56). The methods and procedures documented in this study are specific to this study's objective, aim, and hypothesis.

3.4.1 Ethics

Lawson's Health Research Institute (R-18-631) and the University of Western Ontario's Health Sciences Research Ethics Board (112525) approved this research study (see Appendix C, p. 162-163). All participants consented in writing to take part in the study and received a $25 CAD gift card for their participation.

3.4.2 Design

Quasi-experiment (comparative-control) to detect deficits in driving simulator performance in drivers with MS, as compared to age (±2 years) and sex-matched drivers without MS.

3.4.3 Power

Effect sizes have not yet been established for detecting adjustment to stimuli errors in suburban or urban scenarios in drivers with MS vs. without MS. Accordingly, the sample size for this study was determined based on prior on-road study findings (Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2017). In the prior study, when compared to older drivers with no self-reported medical and neurological disorders (N = 39, M age = 67 years, SD = 1.2), drivers with MS (N = 37, M age = 50 years, SD = 7.3) made 6.1% more driving errors in adjustment to stimuli and gap acceptance (drivers with MS: M = 6.8%, SD = 5.9 vs. older drivers: M = .7%, SD = 1.0; Classen et al., 2018; Krasniuk et al., 2017). Furthermore, more drivers with MS (20%) than without MS (11%) failed the on-road assessment (Classen et al., 2018; Krasniuk et al., 2017). The drivers with MS who failed (vs. passed) made significantly more adjustment to stimuli errors and gap acceptance errors in suburban and urban environments (Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2017).

These prior study findings show that drivers with MS (vs. older drivers) make more adjustment to stimuli errors (i.e., higher event rate), but with more heterogeneity (i.e., larger SD). Though relative validity of driving simulator outcomes with on-road outcomes has not been established in drivers with MS, it has been in other populations (e.g., older drivers, Shechtman et al., 2010; Wynne et al., 2020). Accordingly, based on prior on-road study findings, it was anticipated that drivers with MS would make more simulated adjustment to stimuli errors than drivers without MS. Furthermore, age and sex-matched drivers without MS (vs. older drivers) would have fewer confounding factors on driving performance (United States Department of Transportation & Federal Highway Administration, n.d.).

To control for unequal variance between MS and control groups, the research student used a sampling ratio of two drivers with MS to one driver without MS, matched by age and sex (±2 years; Aberson, 2019, p. 34-53). The prior on-road study findings indicated a small effect (d = .2), thus, not feasible for this study. For adequate statistical power for a medium effect (i.e., differences that would be conceivable to the eye via observation; Portney & Watkins, 2009, p. 831), Green (1991) recommends a minimum $N > 50 + 8k$ (k = number of predictor variables) for tests of multiple regression. Accordingly, in consultation with a biostatistician, and based on the hypothesis (i.e., at least one clinical test to predict), the study needed 40 participants with MS and 20 participants without MS to have a ß = .80 to detect a difference (d = .7) in a one-tailed $alpha$ (α = .05; using independent t-test).

3.4.4 Participants

Participant recruitment, study inclusion and exclusion criteria, and demographic and clinical characteristics of both samples are documented in the prior feasibility study (see

Chapter 2, p. 36, 58). The final sample in this study included 38 fully licensed drivers with MS (*M* age = 42.9 years, *SD* = 10.3, 68% female; 92% relapsing-remitting MS, 8% progressive MS, *median* EDSS score = 2.0, *IQR* = 1.5) and 21 fully licensed drivers without MS (*M* age = 40.0 years, *SD* = 9.9, 71% female).

3.4.5 Procedure

From January 2019 to February 2020, participants individually attended a two-hour in-person visit at the University of Western Ontario's i-Mobile Driving Research Lab. During the visit, participants completed a standardized demographic and medical intake form (Classen et al., 2008), Driver Behaviour Questionnaire (Cordazzo et al., 2014; Reason et al., 1990), visual-cognitive clinical assessment that previously indicated failing an on-road assessment in drivers with MS (Classen, Krasniuk, et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2019; Krasniuk et al., 2017; Morrow et al., 2018), and driving simulator assessment (Alvarez et al., 2019; Alvarez, Classen, Medhizadah, Knott, Asantey, et al., 2018; Alvarez, Classen, Medhizadah, Knott, & He, 2018), administered by the trained research student (see Chapter 2, p. 38-50).

3.4.6 Clinical Measures

For this study, participants' raw scores on the CVLT2-IR and UFOV2 were quantified, as decreased immediate verbal/auditory recall or slower divided attention correlated with simulated adjustment to stimuli errors (operational or tactical) or simulated strategic recall errors in drivers with MS (see Chapter 2, p. 67-69).

3.4.6.1 California Verbal Learning Test-Second Edition

The CVLT2-IR measured participants' immediate verbal/auditory recall through five trials of recalling words on an itemized list (Delis et al., 2000). Test scores included the number of correct responses across five trials out of 80.

3.4.6.2 Useful Field of View™ Subtest 2

As part of a 15-minute computerized test with three subtests (i.e., central visual processing speed, divided attention, selective attention), the UFOV2 measured participants' divided attention and visual processing speed by distinguishing between a car or truck presented in the center of the screen, while concurrently identifying the location of an object in one of eight locations in the periphery of the screen (Visual Awareness Research Group, 2009). Test scores included the mean response accuracy in milliseconds based on accurately responding to 75% of items presented.

3.4.7 Driving Simulator Assessment

Participants completed the driving simulator assessment on the medium-fidelity CDS DriveSafety™ Simulator (DriveSafety™, 2017; Stern et al., 2017, p. 48). The entire driving simulator assessment, including the SAS mitigation protocol, pre-drives, adaptation drives, and main driving scenario is documented in prior studies (see Chapter 2, p. 41-50; Alvarez et al., 2019; Alvarez, Classen, Medhizadah, Knott, Asantey, et al., 2018; Alvarez, Classen, Medhizadah, Knott, & He, 2018). For this study, the research student quantified participants' operational maneuvers in the traffic light event, tactical maneuvers in the pedestrian event, and strategic maneuvers in the navigational driving task of the main driving scenario.

3.4.7.1 Event 2: Traffic Light Changes Colours

The traffic light event recorded participants' operational maneuvers in a suburban environment when responding to a traffic light that suddenly changed from green to yellow and then yellow to red. As the yellow traffic light illuminated, participants responded by either stopping (36% of participants with MS, 62% of participants without MS) or driving through the intersection (64% of participants with MS, 38% of participants without MS; see Chapter 2, p. 66-67).

Participants' adjustment to stimuli was quantified via *maximum response time*, which indicated the time in seconds from when the light illuminated yellow until participants responded to the light by completing stopping or driving through the intersection (Classen, Dickerson, et al., 2017, p. 24; Society of Automotive Engineers International, 2015, p. 35); and *mean speed*, which indicated participants' average traveling speed in meters per second from when the traffic light changed from green to yellow until participants came to a complete stop or drove past the intersection (Classen, Dickerson, et al., 2017, p. 24).

3.4.7.2 Event 3: Pedestrian Walks in Front of Drivers

The pedestrian event recorded participants' tactical maneuvers in an urban environment when responding to verbal directions by the driving simulator to make a right turn while concurrently responding to a pedestrian that suddenly walked across the road in front of them. As the pedestrian started to walk across the road, participants responded by either stopping (83% of participants with MS, 90% of participants without MS) or driving around the pedestrian (17% of participants with MS, 10% of participants without MS; see Chapter 2, p. 66-67).

Participants' adjustment to stimuli was quantified via *reaction time*, which indicated the time in seconds from when the pedestrian started to walk across the road until participants made initial pedal contact (e.g., completely release or initially contact pedal; Classen, Dickerson, et al., 2017, p. 24; Society of Automotive Engineers International, 2015, p. 35); and *maximum response time*, which indicated the time in seconds from when the pedestrian started to walk across the road until participants responded by coming to a complete stop or driving past the pedestrian (Classen, Dickerson, et al., 2017, p. 24; Society of Automotive Engineers International, 2015, p. 35).

3.4.7.3 Navigational Driving Task

The navigational driving task recorded participants' strategic driving maneuvers in an urban environment. The task started once the driving simulator's verbal and visual directions (e.g., directional arrow on monitor screen) disappeared. Participants had to recall the verbal directions provided by the research student at the beginning of the drive (eight to nine minutes prior to the task) to follow the road signs and drive toward London, Ontario, Canada.

Participants' strategic recall maneuvers were quantified via a *correct decision*, i.e., turned toward their destination (80% of participants with MS, 80% of participants without MS), or *incorrect decision*, i.e., drove straight through the intersection (20% of participants with MS, 20% of participants without MS, see Chapter 2, p. 66-67).

3.4.8 Data Analysis

This study includes the same data collection and management procedures as documented in the prior study (see Chapter 2, p. 51-56). All data analyses were computed with SPSS Statistics 26 (IBM Corporation, 2019) using one-sided tests with a significance level α = .05.

Based on preliminary findings (see Chapter 2, p. 66-69), the research student computed five multiple linear or logistic regression models to examine if deficits in immediate verbal/auditory recall (CVLT2-IR) or divided attention (UFOV2) predicted driving performance deficits in participants with MS, as compared to participants without MS. The dependent variables for the models included the following: *model 1* = response type (stopped vs. failed to stop) in the traffic light event; *model 2* = mean speed in meters per second in the traffic light event; *model 3* = reaction time in seconds in the pedestrian event; *model 4* = maximum response time in seconds in the pedestrian event; and *model 5* = correct vs. incorrect decision in the navigational driving task.

Prior to computing regression analyses, the research student tested and met the assumptions of multiple linear regression (i.e., normality, linearity, multicollinearity, homoscedasticity), and reported the findings in Appendix E (p. 170-174). Participants' measures of divided attention on the UFOV2 (score in milliseconds) and maximum response time (seconds) in the traffic light event were not normally distributed. To enter the UFOV2 into a multiple linear regression model without violating the assumption of normality, the research student dichotomized the UFOV2 scores by those lower than the *mean* vs. the *mean* or higher, i.e., scores <29.7 vs. ≥29.7 milliseconds (Warner, 2020, p. 426-442). Likewise, the research student used participants' response type (stopped vs. failed to stop) instead of maximum response time (seconds) and computed a logistic regression model to examine the predictors of the dependent variable.

Through examining multivariate *z*-scores of regression models, the research student identified and removed one multivariate outlier (e.g., *z*-score ±3.3; Warner, 2020, p. 101), as the participant had a maximum response time of 6.0 seconds in the pedestrian event. Accordingly, predictor variables of regression models included group (MS vs. Control), the CVLT2-IR (correct response out of 80), and the UFOV2 (score <29.7 vs. ≥29.7 milliseconds).

For models 2 to 4, the research student performed multiple linear regression models with the backward deletion method, standardized regression coefficients (*Beta weights*), *F*-statistics (*F*), adjusted coefficients of determination ($R^2_{adj.}$), and standard error of the estimate (*SEE*) to examine if the clinical tests can predict driving performance deficits (Portney & Watkins, 2009, p. 691). The backward deletion method entered all predictor variables in the model and deleted variables with the lowest partial correlations until only qualifying predictor variables remained in the model.

For models 1 and 5, the research student performed multiple binary logistic regression with backward deletion method, probabilities of .80, odds ratios (*OR*), and 95% confidence intervals (*CI*), to examine clinical tests predicting participants correct vs. incorrect decisions in the navigational driving task.

3.5 Results

3.5.1 Clinical Tests that Predict Operational Driving Errors in the Traffic Light Event

3.5.1.1 Response Type

Table 3.1 presents the multiple logistic regression model for predicting response type (i.e., stopped vs. failed to stop) in the simulated traffic light event. Neither the CVLT2-IR (correct response out of 80) or UFOV2 (score <29.7 vs. ≥29.7 milliseconds) detected participants' response type in those with MS vs. without MS.

Table 3.1 Multiple Logistic Regression Model for Predicting Response Type in the Traffic Light Event (*N* = 56)

Model	*B*	*SE*	*p*	*OR*	*95% CI for OR*
Step 1					
Group (MS vs. Control)	1.1	.6	.07	2.9	[.9, 9.3]
CVLT2-IR	.0	.0	.22	1.0	[1.0, 1.1]
UFOV2	1.1	.9	.24	2.9	[.5, 16.5]
Step 2					
Group (MS vs. Control)	1.1	.6	.06	3.1	[1.0, 9.7]
CVLT2-IR	.0	.0	.24	1.0	[1.0, 1.1]
Step 3					
Group (MS vs. Control)	1.0	.6	.08	2.8	[.9, 8.4]

Note. Dependent variable: Response type (stopped = 0, failed to stop = 1); Predictor variables: Group (MS = 1; Control = 0); CVLT2-IR (correct response out of 80); UFOV2 (score <29.7 vs. ≥29.7 milliseconds).
Step 1 = *Nagelkerke* R^2= .1, correctly classified = 50.0%.
Step 2 = *Nagelkerke* R^2= .1, correctly classified = 46.4%.
Step 3 = *Nagelkerke* R^2= .1, correctly classified = 46.4%.
B = standardized regression coefficient; *SE* = standard error; *OR* = odds ratio; *CI* = confidence interval for odds ratio; MS = Multiple Sclerosis; CVLT2-IR = California Verbal Learning Test-Second Edition; UFOV2 = Useful Field of View™ Second Subtest.

3.5.1.2 Mean Speed

Table 3.2 presents the multiple linear regression model for predicting mean speed (meters per second) in the simulated traffic light event. Neither the CVLT2-IR (correct response out of 80) or UFOV2 (score <29.7 vs. ≥29.7 milliseconds) detected mean speed in participants with MS or without MS.

Table 3.2 Multiple Linear Regression Model for Predicting Mean Speed in the Traffic Light Event (*N* = 56)

Model	*B*	*SE*	*Beta*	*t*	*p*	*95% CI for B*
Step 1						
Group (MS vs. Control)	.9	.8	.1	1.1	.27	[−.7, 2.4]
CVLT2-IR	.1	.0	.2	1.6	.11	[−.0, .1]
UFOV2	.6	1.1	.1	.5	.59	[−1.6, 2.8]
Step 2						
Group (MS vs. Control)	.9	.8	.1	1.2	.25	[−.6, 2.5]
CVLT2-IR	.1	.0	.2	1.6	.11	[−.0, .1]
Step 3						
CVLT2-IR	.1	.0	.2	1.5	.14	[−.0, .1]

Note. Dependent variable: mean speed in meters per second; Predictor variables: Group (MS = 1; Control = 0); CVLT2-IR (correct response out of 80); UFOV2 (score <29.7 vs. ≥29.7 milliseconds).
Step 1 = F (3, 52) = 1.3, p = .29, R = .3, R^2 = .1, $R^2_{adj.}$ = .0, *SEE* = 2.8, ΔR^2 = .1; constant = 5.8 meters per

second.
Step 2 = F (2, 53) = 1.8, p = .17, R = .3, R^2 = .1, $R^2_{adj.}$ = .0, SEE = 2.8, ΔR^2 = −.0; constant = 6.5 meters per second.
Step 3 = F (1, 54) = 2.2, p = .14, R = .2, R^2 = .0, $R^2_{adj.}$ = .0, SEE = 2.8, ΔR^2 = −.0; constant = 8.3 meters per second.
B = unstandardized regression coefficient; *SE* = standard error; *Beta* = standardized regression coefficient; *t* = independent sample t-test; *CI* = confidence interval for unstandardized regression coefficient; MS = Multiple Sclerosis; CVLT2-IR = California Verbal Learning Test-Second Edition; UFOV2 = Useful Field of View™ Second Subtest; *SEE* = standard error of the estimate.

3.5.2 Clinical Tests that Predict Tactical Driving Errors in the Pedestrian Event

3.5.2.1 Reaction Time

Table 3.3 presents the multiple linear regression model for predicting reaction time (seconds) in the simulated pedestrian event. Slower divided attention (UFOV2 score <29.7 vs. ≥29.7 milliseconds) detected slower reaction time, but not between participants with MS vs. without MS.

Table 3.3 Multiple Linear Regression Model for Predicting Reaction Time in the Pedestrian Event (*N* = 55)

Model	*B*	*SE*	*Beta*	*t*	*p*	*95% CI for B*
Step 1						
Group (MS vs. Control)	−.2	.2	−.2	−1.3	.21	[−.5, .1]
CVLT2-IR	−.0	.0	−.2	−1.6	.12	[−.0, .0]
UFOV2	.5	.2	.3	2.3	.03*	[.1, 1.0]
Step 2						
CVLT2-IR	−.0	.0	−.2	−1.4	.16	[−.0, .0]
UFOV2	.5	.2	.3	2.2	.03*	[.0, 1.0]
Step 3						
UFOV2	.5	.2	.3	2.2	.03*	[.1, 1.0]

Note. Dependent variable: reaction time in seconds; Predictor variables: Group (MS = 1; Control = 0); CVLT2-IR (correct response out of 80); UFOV2 (score <29.7 vs. ≥29.7 milliseconds).
Step 1 = F (3, 51) = 2.9, p = .04, R = .4, R^2 = .1, R^2_{adj}. = .1, SEE = .6, ΔR^2 = .1; constant = 1.8 seconds.
Step 2 = F (2, 52) = 3.6, p = .04, R = .3, R^2 = .1, R^2_{adj}. = .1, SEE = .6, ΔR^2 = −.0; constant = 1.4 seconds.
Step 3 = F (1, 53) = 5.0, p = .03, R = .3, R^2 = .1, R^2_{adj}. = .1, SEE = .6, ΔR^2 = −.0; constant = .7 seconds.
B = unstandardized regression coefficient; *SE* = standard error; *Beta* = standardized regression coefficient; *t* = independent sample t-test; *CI* = confidence interval for unstandardized regression coefficient; MS = Multiple Sclerosis; CVLT2-IR = California Verbal Learning Test-Second Edition; UFOV2 = Useful Field of View™ Second Subtest; *SEE* = standard error of the estimate.
*p ≤.05, one-tailed.

3.5.2.2 Maximum Response Time

Table 3.4 presents the multiple linear regression model for predicting maximum response time (seconds) in the simulated pedestrian event. When compared to control drivers, deficits in immediate verbal/auditory recall (CVLT2-IR correct response out of 80) and slower divided attention (UFOV2 score <29.7 vs. ≥29.7 milliseconds) detected slower maximum response time in participants with MS.

Table 3.4 Multiple Linear Regression Model for Predicting Maximum Response Time in the Pedestrian Event (*N* = 55)

Model	*B*	*SE*	*Beta*	*t*	*p*	*95% CI for B*
Step 1						
Group	.3	.1	.2	2.0	.05*	[.0, .5]
CVLT2-IR	−.0	.0	−.2	−2.0	.05*	[−.0, .0]
UFOV2	.5	.2	.3	2.7	.01*	[.1, .9]

Note. Dependent variable: maximum response time in seconds; Predictor variables: Group (MS = 1; Control = 0); CVLT2-IR (correct response out of 80); UFOV2 (score <29.7 vs. ≥29.7 milliseconds). Step 1 = F (3, 51) = 6.1, p = .001, R = .5, R^2 = .3, $R^2_{adj.}$ = .2, SEE = .5, ΔR^2 = .3; constant = 3.4 seconds. *B* = unstandardized regression coefficient; *SE* = standard error; *Beta* = standardized regression coefficient; *t* = independent sample t-test; *CI* = confidence interval for unstandardized regression coefficient; MS = Multiple Sclerosis; CVLT2-IR = California Verbal Learning Test-Second Edition; UFOV2 = Useful Field of View™ Second Subtest; *SEE* = standard error of the estimate.
*$p \leq .05$, one-tailed.

3.5.3 Clinical Tests that Predict Strategic Driving Errors in the Navigational Driving Task

Table 3.5 presents the multiple logistic regression model for predicting strategic recall errors (correct vs. incorrect decision) in the navigational driving task. Neither clinical test (CVLT2-IR correct response out of 80, UFOV2 score <29.7 vs. ≥29.7 milliseconds) detected correct vs. incorrect decisions in participants with MS vs. participants without MS.

Table 3.5 Multiple Logistic Regression Model for Predicting Correct vs. Incorrect Decision in the Navigational Driving Task (*N* = 54)

Model	*B*	*SE*	*p*	*OR*	*95% CI for OR*
Step 1					
Group (MS vs. Control)	−.2	.7	.75	.8	[.2, 3.4]
CVLT2-IR	−.0	.0	.19	1.0	[.9, 1.0]
UFOV2	1.0	.9	.22	2.9	[.5, 15.4]

Model	*B*	*SE*	*p*	*OR*	*95% CI for OR*
Step 2					
CVLT2-IR	−.0	.0	.20	1.0	[.9, 1.0]
UFOV2	1.0	.8	.23	2.8	[.5, 14.5]
Step 3					
CVLT2-IR	−.0	.0	.18	1.0	[.9, 1.0]

Note. Dependent variable: navigational driving task decision (correct = 0, incorrect = 1); Predictor variables: Group (MS = 1; Control = 0); CVLT2-IR (correct response out of 80); UFOV2 (score <29.7 vs. ≥29.7 milliseconds).
Step 1 = *Nagelkerke* R^2 = .1, correctly classified = 79.6%.
Step 2 = *Nagelkerke* R^2 = .1, correctly classified = 79.6%.
Step 3 = *Nagelkerke* R^2 = .1, correctly classified = 79.6%.
B = standardized regression coefficient; *SE* = standard error; *OR* = odds ratio; *CI* = confidence interval for odds ratio; MS = Multiple Sclerosis; CVLT2-IR = California Verbal Learning Test-Second Edition; UFOV2 = Useful Field of View™ Second Subtest.

3.6 Discussion

This study examined if clinical tests (i.e., CVLT2-IR, UFOV2) can detect adjustment to stimuli errors (operational and/or tactical) and/or strategic recall errors on a driving simulator in drivers with MS. Study findings supported the hypothesis: when compared to control drivers without MS, deficits in immediate verbal/auditory recall (CVLT2-IR) and slower divided attention (UFOV2) predicted tactical adjustment to stimuli errors (i.e., slower maximum response time) in drivers with MS. Specifically, drivers with MS took longer to completely stop or pass the pedestrian that walked out in front of them. Also, drivers with verbal/auditory recall deficits took longer or did not recall prior information, such as the verbal instructions to observe road users not following the rules, and as such took longer to respond to the pedestrian. Furthermore, drivers with slower divided attention took longer to visually search and scan, detect, attend, judge, initiate, and respond to critical roadway information.

These findings suggest that the CVLT2-IR and UFOV2 may capture the visual and verbal/auditory recall, processing speed, and divided attention required to respond to the pedestrian. Notably, the pedestrian event requires drivers to attend to multiple visual and auditory stimuli, including the verbal directions provided by the driving simulator to turn right, while concurrently responding to the pedestrian who randomly walked out in front. While drivers mentally processed the verbal directions, they began to initiate a lane change, and then responded by either braking or driving around the pedestrian.

Conversely, the traffic light event and navigational driving task may not have required verbal/auditory recall or divided attention like in the pedestrian event. The traffic light event required participants to respond via stopping or driving straight through the intersection. Accordingly, this may be one explanation for why immediate verbal/auditory recall (CVLT2-IR) or divided attention (UFOV2) did not detect operational adjustment to stimuli errors (i.e., response type, mean speed) in this event. Another explanation may be that such operational maneuvers may not underlie driving performance deficits in drivers with MS.

The navigational driving task required drivers to recall the prior directions and make a right turn toward London, Ontario, Canada. Accordingly, the task may not have required divided attention, which may be one reason why the UFOV2 did not detect incorrect (vs. correct) decisions in those with MS and without MS. In the prior feasibility study, decreased immediate verbal/auditory recall (CVLT2-IR) correlated with incorrect decisions in drivers with MS. However, most drivers (80%) made a correct decision. Accordingly, the prior and current findings suggest that the navigational driving task may not have challenged strategic driving maneuvers in drivers with MS, when compared to control drivers without MS. As such, the CVLT2-IR or UFOV2 may not detect these strategic recall errors.

Consistent with findings in the literature, impairment in divided attention and visual processing speed may indicate driving performance deficits in drivers with MS (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Classen et al., 2018; Devos et al., 2013; Devos et al., 2017; Harand et al., 2018; Kotterba et al., 2003; Lincoln & Radford, 2008; Marcotte et al., 2008; Morrow et al., 2018; Schultheis et al., 2010). In addition, this study also found that impairment in verbal/auditory recall may detect driving performance. Furthermore, tactical adjustment to stimuli errors (vs. operational or strategic errors) may underlie driving performance deficits when drivers with MS undergo a driving simulator assessment. As such, based on prior and current study findings, immediate verbal/auditory recall and divided attention may be useful clinical indicators of driving performance in drivers with MS.

3.6.1 Limitations

Besides the limitations identified in the prior feasibility study (e.g., selection bias, spectrum bias, observer bias, missing data, see Chapter 2, p. 74), this study contained additional limitations. The preliminary feasibility findings may not have detected significant differences or relationships, as the aim of the feasibility study was to understand the feasibility of utilizing clinical tests that may indicate driving simulator performance in drivers with MS. In addition, missing data resulted in quantifying predictions with 54 and 56 participants vs. the anticipated 60 participants, which may have underestimated the actual results that could have been obtained from a sample of 60. The study only examined if visual and cognitive impairment, via clinical tests, contributed to driving simulator performance. Other characteristics (e.g., demographic, onset of simulator adaptation syndrome) that were not examined may also contribute to participants' driving performance.

3.6.2 Strengths

In addition to the strengths identified in the prior feasibility study (e.g., supervisory and consultative teams, kinematic data on driving simulator, see Chapter 2, p. 75), this study contained additional strengths. The findings of this study contribute to the clinical indicators of driving maneuvers that may underlie driving simulator performance deficits in drivers with MS. The study included an adequately powered sample of drivers with MS and a control group of drivers without MS. Further, the study used maximum response time to indicate adjustment to stimuli errors in drivers with MS. Typically, reactions and responses are reported in summary measures of means across trials (Society of Automotive Engineers International, 2015, p. 9), which would not provide adequate insight into identifying errors of operational, tactical, or strategic driving maneuvers. As the study had additional measures to indicate adjustment to stimuli errors, findings elucidated that drivers with MS have difficulty in tactical (vs. operational or strategic) maneuvers.

3.6.3 Implications for Research

This study supports the notion that impairment in immediate verbal/auditory recall and slower divided attention may underlie impaired driving simulator performance in drivers with MS. Understanding other factors (e.g., demographics, driving exposure) that contribute to participants' driving performance may validate decisions about one's driving performance. Further, the visual-cognitive impairment that cause deficits in driving performance are not fully understood. Understanding the causal factors that affect driving performance is important for developing targeted intervention protocols to remediate impairments underlying driving performance.

3.6.4 Implications for Clinical Practice

In this study, deficits in immediate verbal/auditory recall (CVLT2-IR) and divided attention (UFOV2) detected driving simulator performance in drivers with MS. Implementing the CVLT2-IR and UFOV may provide information for understanding the role of episodic immediate verbal/auditory recall and divided attention on driving performance. Such tests may be used to screen for at-risk drivers and design treatment plans to compensate or remediate for such difficulty. The CVLT2-IR takes about 5 to 10 minutes to complete and costs about $250 USD for the administration manual and test scoring forms. The UFOV takes about 15 minutes to complete and costs about $4100 USD. Currently, the standards for determining fitness to drive do not include specific assessments. Clinicians are encouraged to be cognizant of, and use practices, consistent and informed by best evidence, as shown through this work.

Study findings suggest that the complexity in hazardous events may influence operational and tactical driving maneuvers of drivers with MS. For example, driving through a yellow traffic light would not be as severe as hitting a pedestrian that suddenly walked in front of drivers on the road. Depending on the driver's location and when the traffic light changed, driving through the light was the less severe action to take. Deficits in operational driving maneuvers may be remediated through compensatory strategies. For example, teaching the driver strategies (e.g., scanning the environment) to anticipate and prepare slowing down when approaching intersections. Alternatively, using a driver assistance system that automatically recognizes traffic signals and that alert the driver may be a plausible strategy. However, the use and benefit of such strategies have not yet been empirically tested in the MS population.

3.7 Conclusion

This study examined if immediate verbal/auditory recall and divided attention can predict adjustment to stimuli errors (operational or tactical) and/or strategic recall errors on a driving simulator in drivers with MS, as compared to control drivers without MS. When compared to drivers without MS, deficits in immediate verbal/auditory recall and slower divided attention detected tactical adjustment to stimuli errors (vs. operational or strategic errors) in drivers with MS. The CVLT2-IR and UFOV2 may capture the visual and verbal/auditory recall, processing speed, and divided attention required to respond to stimuli of tactical maneuvers. Clinicians may consider screening for deficits in immediate verbal/auditory recall and divided attention to identify driving performance deficits. The CVLT2-IR and UFOV2 may be useful clinical indicators of driving simulator performance in drivers with MS.

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Chapter 4

4 Driving Errors that Predict Simulated Rear-End Collisions in Drivers with Multiple Sclerosis

Worldwide, road traffic crashes injure over 50 million individuals and kill over 1 million individuals each year (World Health Organization, 2018). As a medically at-risk population, drivers with MS have an increased risk for crash involvement. When compared to drivers without MS, drivers with MS have higher rates of road traffic offences, injuries, and crashes (Brønnum-Hansen et al., 2006; Dehning et al., 2014; Lings, 2002). Notably, Dehning et al. (2014) found that drivers with MS had more total driving offences on their driving record (drivers with MS, N = 35, M = 1.6, SD = 2.6, vs. drivers without MS, N = 35, M = .5, SD =.7, F (1, 68) = 5.9, p =.02). Lings (2002) found that drivers with MS had 3.4 times more traffic injuries that resulted in emergency departments (drivers with MS, 5/197 vs. drivers without MS, 4/545, 95% *confidence interval* = [.7, 17.2], p = .04, one-tailed). Furthermore, Brønnum-Hansen et al. (2006) found that road traffic crashes contributed to 20% of all fatal accidents (e.g., traffic, poisoning, falls, burns, suffocation, other) in individuals with MS. Though these study findings may be alarming, the driving performance deficits that contribute to crashes has not been extensively studied. Assessing crashes in an on-road assessment could be considered unsafe for road users (Yuen et al., 2012). However, assessing crashes on a driving simulator may safely inform whether the same driving performance deficits underlie fitness to drive and simulated crashes (Lew et al., 2009; Shechtman, 2010; Wynne et al., 2019). Therefore, this study aims to examine if the underlying driving performance impairments of on-road driving can also contribute to the occurrence of crashes on a driving simulator.

Based on the extant literature, adjustment to stimuli errors in suburban and urban environments indicate failing an on-road assessment (Classen, Krasniuk, et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2017). In the prior feasibility study, more drivers with MS (34%) vs. without MS (10%) experienced a rear-end collision with a vehicle that cut across the lane in front of them (*Cramer's V* = .3, p = .04;

see Chapter 2, p. 66-67). Building on the literature, these preliminary findings suggest that adjustment to stimuli errors may indicate on-road and simulated driving performance impairment in drivers with MS. Therefore, this study will examine whether adjustment to stimuli errors contribute to the occurrence of simulated collisions in drivers with MS, as compared to those without MS. If the same deficits contribute to on-road outcomes and the occurrence of collisions, assessors may use such information to guide their fitness to drive decision-making.

4.1 Objective

This study will examine if adjustment to stimuli errors can detect the occurrence of rear-end collisions on a driving simulator in drivers with MS.

4.2 Aims

The aim of this study is twofold: 1) Quantify if adjustment to stimuli errors can predict the occurrence of rear-end collisions on a driving simulator in drivers with MS, as compared to control drivers without MS; and 2) Quantify the predictive validity and optimal cut-points of adjustment to stimuli errors for detecting rear-end collisions in both groups.

4.3 Hypothesis

Adjustment to stimuli errors indicate failing an on-road assessment in drivers with MS (Classen, Krasniuk, et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2017). Therefore, it is hypothesized that, when compared to drivers without MS, adjustment to stimuli errors will detect the occurrence of simulated rear-end collisions in drivers with MS.

4.4 Methods

This study includes the same methods and procedures as documented in the prior feasibility study (see Chapter 2, p. 36-56). The methods and procedures documented in this study are specific to this study's objective, aim, and hypothesis.

4.4.1 Ethics

Lawson's Health Research Institute (R-18-631) and the University of Western Ontario's Health Sciences Research Ethics Board (112525) approved this research study (Appendix C, p. 162-163). All participants consented in writing to take part in the study and received a $25 CAD gift card for their participation.

4.4.2 Design

Quasi-experiment (comparative-control) to detect driving simulator performance in drivers with MS, as compared to age (±2 years) and sex matched drivers without MS.

4.4.3 Participants

Participant recruitment, study inclusion and exclusion criteria, and demographic and clinical characteristics of both samples are documented in the prior feasibility study (see Chapter 2, p. 36, 58). The final sample in this study included 38 fully licensed drivers with MS (*M* age = 42.9 years, *SD* = 10.3, 68% female) and 21 fully licensed drivers without MS (*M* age = 40.0 years, *SD* = 9.9, 71% female).

4.4.4 Procedure

Participants individually attended a two-hour in-person visit at the University of Western Ontario's i-Mobile Driving Research Lab where they completed a standardized demographic and medical intake form (Classen et al., 2008), Driver Behaviour Questionnaire (Cordazzo et al., 2014; Reason et al., 1990), visual-cognitive clinical assessment that previously indicated failing an on-road assessment in drivers with MS (Classen, Krasniuk, et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2019; Krasniuk et al., 2017; Morrow et al., 2018), and a driving simulator assessment (Alvarez et al., 2019; Alvarez, Classen, Medhizadah, Knott, Asantey, et al., 2018; Alvarez, Classen, Medhizadah, Knott, & He, 2018), administered by the trained research student (see Chapter 2, p. 38-50).

4.4.4.1 Driving Simulator

Participants completed the driving simulator assessment on the medium-fidelity CDS DriveSafety™ Simulator (DriveSafety™, 2017; Stern et al., 2017, p. 48). The entire driving simulator assessment, including the SAS mitigation protocol, pre-drives, adaptation drives, and main driving scenario is documented in prior studies (see Chapter 2, p. 41-50; Alvarez et al., 2019; Alvarez, Classen, Medhizadah, Knott, Asantey, et al., 2018; Alvarez, Classen, Medhizadah, Knott, & He, 2018). For this study, the research student quantified participants' tactical maneuvers and the occurrence of rear-end collisions in *event 4, when the vehicle cut across the lane in front of drivers*, as the event was the sole location of collisions.

4.4.4.1.1 Event 4: Vehicle Cuts Across Lane in Front of Drivers

This event recorded participants' tactical driving maneuvers in an urban environment when responding to a vehicle that cut across the lane in front of them. As the vehicle started to cross into the lane, participants either stopped (56% participants with MS, 70% participants without MS), drove around the vehicle (6% participants with MS, 20% participants without MS), or experienced a rear-end collision (38% participants with MS, 10% participants without MS, see Chapter 2, p. 66-67).

Participants' adjustment to stimuli was quantified via *reaction time*, *time to collision*, and *mean speed*. *Reaction time* indicated the time in seconds from when the vehicle started to cut across the lane until participants made initial pedal contact (e.g., complete pedal release or initial pedal contact; Classen, Dickerson, et al., 2017, p. 24; Society of Automotive Engineers International, 2015, p. 35). *Time to collision* indicated the time in seconds to a collision (Society of Automotive Engineers International, 2015, p. 54). *Mean speed* indicated the participants' average traveling speed in meters per second from when the vehicle cut across the lane until participants made a complete stop, drove past the vehicle, or experienced a collision.

4.4.5 Data Analysis

This study includes the same data collection and management procedures as documented in the prior study (see Chapter 2, p. 51-56). All data analyses were computed with SPSS Statistics 26 (IBM Corporation, 2019) using two-sided tests with a significance level $\alpha = .05$. Spearman rho (r_s) or rank biserial correlations (r_{rb}) quantified the strength and direction of bivariate correlations between reaction time (seconds), time to collision (seconds), or mean speed (meters per second) and the occurrence of rear-end collisions (collide vs. did not collide; Portney, 2020, p. 435). Correlations with values <.30 were weak; .30 to .69 were moderate; and .70 to 1.00 were strong to perfect (Jackson, 2009, p. 142).

Univariate logistic regression analyses with direct entries, probabilities of .80, odds ratios (*OR*), and 95% confidence intervals (*CI*) were computed to quantify if reaction time, time to collision, and/or mean speed predicted the occurrence of rear-end collisions (Portney & Watkins, 2009, p. 697-698). For each significant predictor, a receiver operating characteristics (ROC) curve was plotted and the area under the curve (AUC; criteria ≥.70, $p \leq .05$) was computed to quantify the driving error's (i.e., reaction time, time to collision, mean speed) probability of correctly distinguishing between those who collided vs. did not collide (Streiner & Cairney, 2007).

For each ROC curve, cut-points of reaction time, time to collision, or mean speed were computed to quantify their classification indicators for detecting the occurrence of rear-end collisions, i.e., *sensitivities*, *specificities*, *positive predictive values*, *negative predictive values*, *misclassifications*, and *error rates* (Portney, 2020, p. 509-528). Table 4.1 describes the classification indicators for reaction time, time to collision, and mean speed.

Sensitivity pertains to the test's ability (e.g., cut-point of reaction time, time to collision, mean speed) to detect the presence of a collision when a collision truly occurred (Portney, 2020, p. 511). *Specificity* pertains to the test's ability (e.g., cut-point of reaction time, time to collision, or mean speed) to detect the absence of a collision when a collision truly did not occur (Portney, 2020, p. 511).

Positive predictive value pertains to the driver's score in reaction time, time to collision, or mean speed detected by the test (e.g., cut-point) to indicate the presence of a collision (Portney, 2020, p. 513). *Negative predictive value* pertains to the driver's score in reaction time, time to collision, or mean speed detected by the test (e.g., cut-point) to indicate the absence of a collision (Portney, 2020, p. 513).

Misclassifications pertain to the test's (e.g., cut-point of reaction time, time to collision, or mean speed) measurement error by summing the number of *false positives* (e.g., incorrect classification for detecting the presence of collisions) and *false negatives* (e.g., incorrect classification for detecting the absence of collisions; Krzanowski & Hand, 2009). *Error rate* quantifies the test's measurement error when sensitivity and specificity have equal weight (error rate = [1 − sensitivity] + [1 − specificity]; Krzanowski & Hand, 2009). *Optimal cut-points* comprised those with the lowest error rate.

Table 4.1 Description of Classification Indicators for Adjustment to Stimuli Detecting the Occurrence of Rear-End Collisions on a Driving Simulator

Adjustment to stimuli	Cut-Point Indicators			
	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
Reaction time (seconds)	The proportion of participants with the same reaction time or slower reaction time than the cut-point's score out of all who collided.	The proportion of participants with a faster reaction time than the cut-point's score out of all who did not collide.	The proportion of participants who collided out of all participants with the same reaction time or slower reaction time than the cut-point's score.	The proportion of participants who did not collide out of all participants with a faster reaction time than the cut-point's score.
Time to collision (seconds)	The proportion of participants with the same time to collision or shorter time to collision than the cut-point's score out of all who collided.	The proportion of participants with a longer time to collision than the cut-point's score out of all who did not collide.	The proportion of participants who collided out of all participants with the same time to collision or shorter time to collision than the cut-point's score.	The proportion of participants who did not collide out of all participants with a longer time to collision than the cut-point's score.
Mean speed (meters per second)	The proportion of participants with the same mean	The proportion of participants with a slower mean	The proportion of participants who collided out of all	The proportion of participants who did not collide out

Adjustment to stimuli	Cut-Point Indicators			
	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
	speed or faster mean speed than the cut-point's score out of all who collided.	speed than the cut-point's score out of all who did not collide.	participants with the same mean speed or faster mean speed than the cut-point's score.	of all participants with a slower mean speed than the cut-point's score.

4.5 Results

4.5.1 Rear-End Collisions on a Driving Simulator

Table 4.2 presents the bivariate correlations of participants' reaction time (seconds), time to collision (seconds), or mean speed (meters per second) and the occurrence of rear-end collisions (collide vs. did not collide) when the simulated vehicle cut across the lane in front of them. A shorter time to collision and a faster mean speed correlated with experiencing a rear-end collision, but they also correlated with one another. To eliminate multicollinearity, univariate logistic regressions were computed with time to collision and mean speed as sole predictors of rear-end collisions.

Table 4.2 Bivariate Correlations Between Adjustment to Stimuli Errors and Rear-End Collisions on a Driving Simulator (*N* = 54)

Driving simulator outcomes	1a	2b	3b	4
1. Rear-end collisions (collided vs. did not collide)	—			
2. Reaction time (seconds)	−.0	—		
3. Time to collision (seconds)	−.6**	.2	—	
4. Mean speed (meters per second)	.4**	.1	−.3*	—

Note. Predictor variable: Rear-end collision (collided = 1 vs. did not collide = 0).
aRank biserial correlations; bSpearman rho correlations.
**$p \leq .001$, two-tailed, *$p \leq .05$, two-tailed.

Table 4.3 summarizes two univariate logistic regression models to examine the occurrence of simulated rear-end collisions. As sole predictors, a shorter time to collision (seconds) and a faster mean speed (meters per second) detected the occurrence of rear-end collisions in participants with MS (vs. participants without MS).

Table 4.3 Univariate Binary Logistic Regression Models for Predicting Rear-End Collisions on a Driving Simulator (*N* = 54)

Univariate Regression Model	*B*	*SE*	*OR*	*p*	*95% CI for OR*
Model 1					
Group (MS vs. Control)	4.7	1.8	104.3	.009*	[3.2, 3365.7]
Time to collision (seconds)	−3.2	1.0	.0	.001*	[.0, .3]
Model 2					
Group (MS vs. Control)	2.2	1.0	9.1	.02*	[1.4, 59.8]
Mean speed (meters per second)	.3	.1	1.3	.04*	[1.0, 1.7]

Note. Dependent variable: occurrence of simulated rear-end collisions (collided = 1, did not collide = 0).
Predictor variable: Group (MS = 1 vs. Control = 0).
Model 1: *Nagelkerke* R_2 = .7, Accurately classified 92.6% of collisions.
Model 2: *Nagelkerke* R_2 = .3. Accurately classified 72.2% of collisions.
B = standardized regression coefficient; *SE* = standard error; *OR* = odds ratio; *CI* = confidence interval for odds ratio.
*$p \leq .05$, two-tailed.

4.5.2 Cut-Points of Driving Errors that Detect Rear-End Collisions on a Driving Simulator

4.5.2.1 Time to Collision

Figure 4.1 and Figure 4.2 present the ROC curves plotting the predictive validity of time to collision (seconds) for detecting the occurrence of rear-end collisions in participants with MS (see Figure 4.1) and in participants without MS (see Figure 4.2). Time to collision predicted 94% of rear-end collisions in participants with MS (*AUC* = .94, $p < .0001$, *SE* = .05, *95% CI* = [.9, 1.0]), and 86% of rear-end collisions in those without MS (*AUC* = .86, $p < .0001$, *SE* = .08, *95% CI* = [.7, 1.0]). The non-significant area difference under the ROC curve showed that time to collision as a test detected collisions in both groups ($z = -.8$, $p = .41$, *AUC difference* = −.1, *SE difference* = .1, *95% CI* = [−.3, .1]).

For participants with MS, a time to collision cut-point ≤1.8 seconds optimally predicted rear-end collisions with 85% sensitivity (11/ 13), 100% specificity (21/ 21), 100% positive predictive value (11/ 11), 91% negative predictive value (21/ 23), 2 misclassifications (0 false positives, 2 false negatives), and 15% error rate. For participants without MS, a time to collision cut-point ≤1.3 seconds optimally predicted rear-end collisions with 100% sensitivity (2/ 2), 83% specificity (15/ 18), 40% positive predictive value (2/ 5), 100% negative predictive value (15/ 15), 3 misclassifications (3 false positives, 0 false negatives), and 17% error rate.

4.5.2.2 Mean Speed

Figure 4.3 and Figure 4.4 present the ROC curves plotting the predictive validity of mean speed (meters per second) for detecting the occurrence of rear-end collisions in participants with MS (see Figure 4.3) and in participants without MS (see Figure 4.4). Mean speed predicted 76% of rear-end collisions in participants with MS (*AUC* = .76, *p* = .005, *SE* = .1, *95% CI* = [.6, 9]); and 78% of rear-end collisions in participants without MS (*AUC* = .78, *p* = .005, *SE* = .1, *95% CI* = [.6, .9]). The non-significant area difference under the ROC curve showed that mean speed as a test detected collisions in both groups (*z* = .2, *p* = .86, *AUC difference* = .0, *SE difference* = .1, *95% CI* = [−.2, .3]).

For participants with MS, a mean speed cut-point ≥7.8 meters per second optimally predicted simulated rear-end collisions with 77% sensitivity (10/ 13), 76% specificity (16/ 21), 67% positive predictive value (10/ 15), 84% negative predictive value (16/ 19), 8 misclassifications (5 false positives, 3 false negatives), and 47% error rate. For participants without MS, a mean speed cut-point ≥10.4 meters per second optimally predicted simulated rear-end collisions with 100% sensitivity (2/ 2), 78% specificity (14/ 18), 33% positive predictive value (2/ 6), 100% negative predictive value (14/ 14), 4 misclassifications (4 false positives, 0 false negatives), and 22% error rate.

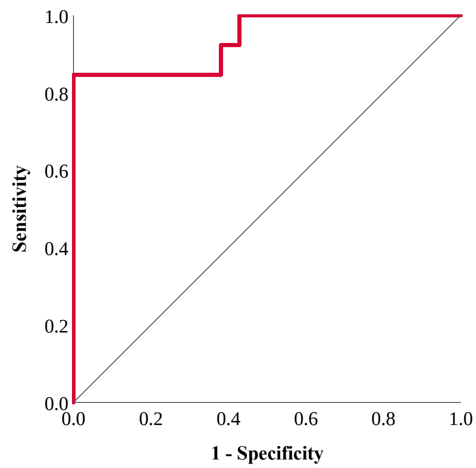

Figure 4.1 Predictive Validity of Time to Collision (in seconds) for Detecting Rear-End Collisions on a Driving Simulator in Participants with Multiple Sclerosis (*N* = 34)

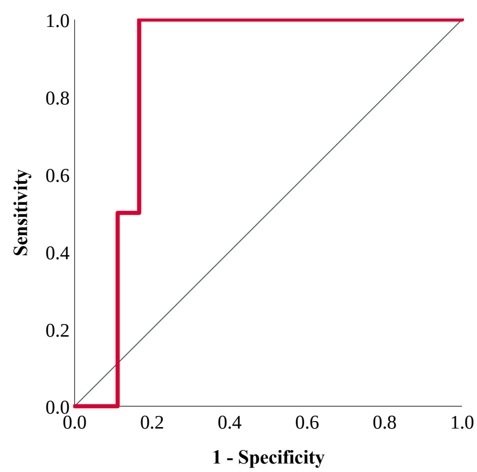

Figure 4.2 Predictive Validity of Time to Collision (in seconds) for Detecting Rear-End Collisions on a Driving Simulator in Participants without Multiple Sclerosis (*N* = 20)

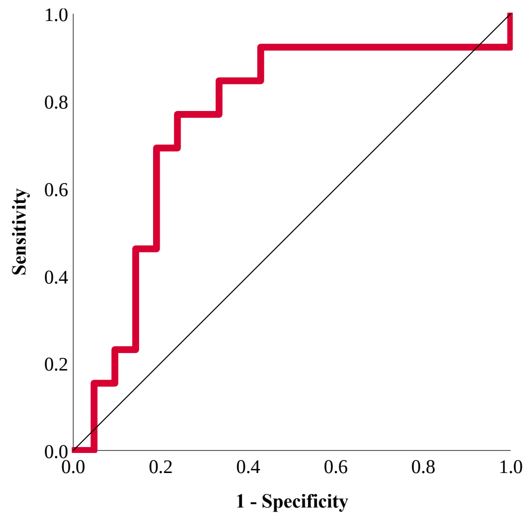

Figure 4.3 Predictive Validity of Mean Speed (in meters per second) for Detecting Rear-End Collisions on a Driving Simulator in Participants with Multiple Sclerosis (*N* = 34)

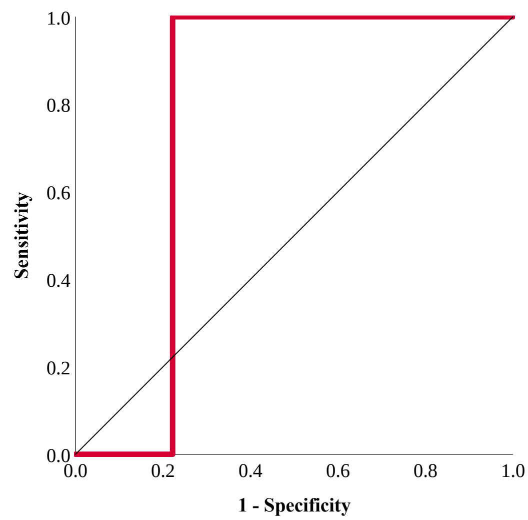

Figure 4.4 Predictive Validity of Mean Speed (in meters per second) for Detecting Rear-End Collisions on a Driving Simulator in Participants without Multiple Sclerosis (*N* = 20)

4.6 Discussion

This study examined if simulated adjustment to stimuli errors can detect the occurrence of simulated rear-end collisions in drivers with MS, when compared to drivers without MS. Study findings supported the hypothesis: as sole predictors, a shorter time to collision and a faster mean speed detected the occurrence of simulated rear-end collisions in drivers with MS. Though reaction time did not detect collisions in either group, the outcome measure did not differentiate between participants' initial contact with the accelerator or brake pedal. However, prior feasibility findings showed that every driver who experienced a collision failed to come to a complete stop (see Chapter 2, p. 66-67). Accordingly, an explanation may be that drivers initially reacted via pressing the accelerator pedal; or, drivers did not respond in enough time to come to a complete stop and avoid a collision. Though inferences cannot be made toward initial accelerator or brake pedal contact, these findings indicate that more drivers with MS than without MS failed to respond to the stimuli at an appropriate pace for the urban environment. Accordingly, drivers did not have enough time or drove too fast to avoid a collision when the vehicle cut across the lane in front of them. As such, adjustment to stimuli errors can detect rear-end collisions on a medium-fidelity driving simulator in drivers with MS.

The ROC curve analyses showed that time to collision (see Figure 4.1 and Figure 4.2) and mean speed (see Figure 4.3 and Figure 4.4) detected the occurrence of rear-end collisions in drivers with MS and in drivers without MS. Time to collision had higher predictive validity than mean speed, and both measures detected collisions in both groups. When compared to those without MS, a longer time to collision and a slower mean speed optimally detected collisions in driver with MS. These findings indicate that drivers with MS who experienced a collision did not process or respond to the vehicle that crossed the lane in front of them even though they had more time and drove slower than those without MS. However, as measurement error exists in both optimal cut-points, the time to collision and mean speed must be interpreted with caution and to support evidence-informed clinical judgment when making driving performance decisions.

Consistent with the literature, this study showed that adjustment to stimuli errors may underlie driving performance deficits in drivers with MS (Classen, Krasniuk, et al., 2017;

Classen et al., 2018; Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003; Krasniuk et al., 2020; Krasniuk et al., 2017). Drivers did not process the demands posed by the environment in a timely manner, which resulted in a shorter time to collision, faster mean speed, and rear-end collisions. These findings elucidate the processing speed impairment that may contribute to understanding collisions on a driving simulator.

4.6.1 Limitations

This study has limitations in addition to those identified in the prior feasibility study (see Chapter 2, p. 74) and clinical prediction study (see Chapter 3, p. 96). Compared to an on-road driving assessment, a driving simulator is a plausible substitute for determining driving performance of medically at-risk drivers; however, it does not measure real-world driving (Caffò et al., 2020; Shechtman, 2010; Wynne et al., 2019). As such, driving performance on a simulator cannot be used to solely determine someone's fitness to drive, and crashes on a driving simulator cannot directly relate to crashes in real-world driving (Caffò et al., 2020; Wynne et al., 2019).

4.6.2 Strengths

Likewise, this study has strengths in addition to those identified in the prior feasibility study (see Chapter 2, p. 75) and clinical prediction study (see Chapter 3, p. 96). This study brought novel insight to understanding the driving errors of those with MS that contribute to experiencing collisions on a driving simulator—via a safe, prospective and objective assessment of their driving performance. As adjustment to stimuli errors detect decreased on-road outcomes, these findings suggest that time to collision and mean speed may identify the occurrence of collisions when performing tactical maneuvers that require a pedal response.

4.6.3 Implications

In this study, shorter time to collision and faster mean speed, which is suggested to indicate a failed response, predicted rear-end collisions. As a driving simulator provides a safe, crash-free assessment of driving behaviours, clinicians may want to consider assessing driving performance deficits in drivers with MS on a simulator prior to an on-road assessment. Clinicians may also want to consider the effect of participants' time to collision and mean speed on driving performance and tailor assessment and intervention strategies accordingly.

4.6.4 Conclusion

This study concluded that tactical adjustment to stimuli errors in urban environments may underlie driving simulator performance deficits in drivers with MS. Such driving errors measured via mean speed and time to collision can detect rear-end collisions on a driving simulator. Drivers who experienced a collision failed to respond to the environment at an adequate pace to avoid a collision. These findings highlight the processing speed impairments of drivers with MS that may impact their driving abilities and behaviours. Assessors may target tactical adjustment to stimuli errors in urban environments to help inform their decisions about one's driving performance on a simulator.

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Chapter 5

5 Discussion

Based on prior on-road study findings (Classen et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2019; Krasniuk et al., 2017; Morrow et al., 2018), this dissertation examined the clinical utility of visual and cognitive tests to indicate driving simulator performance in drivers with MS, when compared to drivers without MS. The dissertation had three aims. The first aim examined the feasibility of the study via evaluating: 1) Recruitment capability and resulting sample characteristics; 2) Data collection procedures and outcome measures; 3) The acceptability and suitability of the driving simulator; 4) The resources and ability to manage and implement the study; and 5) Preliminary clinical and driving simulator test results (see Chapter 2, p. 34-82).

The second aim examined if the clinical tests (BVMTR-IR, BVMTR-DR, CVLT2-IR, SDMT, UFOV, and far-sighted binocular visual acuity) can indicate operational and/or tactical adjustment to stimuli errors, and/or strategic recall errors on a driving simulator in drivers with MS (see Chapter 3, p. 83-102). On-road study findings indicate that at least one of these clinical tests predict failing outcomes in drivers with MS (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Devos et al., 2017; Krasniuk et al., 2019; Morrow et al., 2018; Ranchet et al., 2015; Schultheis et al., 2010). Accordingly, it was hypothesized that impairment in at least one clinical test would predict simulated driving errors in drivers with MS.

Lastly, the third aim examined if adjustment to stimuli errors can detect the occurrence of rear-end collisions on a driving simulator (see Chapter 4, p. 103-120). As on-road study findings show that adjustment to stimuli errors indicate drivers with MS failing an on-road assessment (Classen et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2017), it was hypothesized that simulated adjustment to stimuli errors would predict simulated rear-end collisions in drivers with MS, when compared to those without MS.

Overall, findings for the first aim showed that utilizing visual and cognitive clinical tests indicative of decreased on-road outcomes can also indicate deterioration in driving simulator performance in drivers with MS. Notably, these findings concluded that it was feasible to carry out an adequately powered study with the CVLT2-IR and UFOV2 as predictor variables of driving simulator performance in drivers with MS vs. without MS. However, these findings also identified common challenges associated with driving simulator studies for neurologically at-risk drivers, e.g., those with MS. Findings for the second aim supported the hypothesis, as deficits in immediate verbal/auditory recall (CVLT2-IR) and slower divided attention (UFOV2) detected simulated tactical adjustment to stimuli errors in drivers with MS. Furthermore, findings for the third aim supported the hypothesis, as simulated adjustment to stimuli errors detected the occurrence of rear-end collisions in drivers with MS. This chapter addresses the dissertation's key findings and discusses their contributions to the literature, highlights the limitations and strengths that may have impacted study findings, and provides implications for research, policy, and clinical practice.

5.1 Feasibility of Utilizing Clinical Tests to Predict Driving Simulator Performance in Drivers with Multiple Sclerosis

5.1.1 Evaluate Recruitment Capability and Resulting Sample Characteristics

The feasibility study showed low recruitment rates when compared to proposed rates for participants with MS, who mostly comprised individuals with relapsing-remitting MS and low physical disability recruited via the London (Ontario) MS Clinic. One reason for low recruitment rates may include a fear of license loss (Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Archer et al., 2014; Morrow et al., 2018). In jurisdictions like Canada, healthcare professionals, including physicians, nurse practitioners, occupational therapists, and optometrists, have a discretionary or mandatory responsibility to report at-risk drivers to the Ministry of Transportation or Department of Motor Vehicles (Canadian Council of Motor Transport Administrators, 2020, p. 8; Canadian Medical Association, 2019, p. 11-15). When recruiting participants, researchers with these professional backgrounds who are registered with their respective college must discuss the implications of study procedures (e.g., on-road assessment) on reporting, which can include completing a CDE at the drivers' expense with license revocation as a possible outcome (Canadian Council of Motor Transport Administrators, 2020, p. 42-49; Canadian Medical Association, 2019, p. 16-19). Individuals who experience an increased anxiety or fear for losing their license may thus become reluctant to take part, and as such, decline their participation (Archer et al., 2014).

Though findings in this study did not show that individuals declined for this reason, a fear for license revocation is documented in the literature (Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Morrow et al., 2018). Notably, Morrow et al. (2018) report that about 25% of recruited participants with MS decided not to participate for fear of losing their license. Furthermore, Akinwuntan, Devos, et al. (2012) and Akinwuntan, O'Connor, et al. (2012) report that 8% (4/ 49) of participants with relapsing-remitting MS opted out of the on-road assessment because they were concerned of the legal implications for obtaining a failing outcome. Though reported anecdotally, a fear of license loss is likely a limitation when recruiting neurologically at-risk drivers to participate in studies that take place in jurisdictions with a responsibility to report.

Though driving studies do not often report on recruitment goals, they often report on small sample sizes of individuals with similar characteristics to those reported in the feasibility study (Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Classen et al., 2018; Devos et al., 2013; Harand et al., 2018; Kotterba et al., 2003; Krasniuk et al., 2019; Lamargue-Hamel et al., 2015; Lincoln & Radford, 2008; Marcotte et al., 2008; Morrow et al., 2018; Raphail et al., 2020; Schultheis et al., 2010; Schultheis et al., 2009). These findings may be problematic for two reasons: i.e., type II error may result from not having adequate sample sizes to detect significant indicators of driving performance; and study findings may only generalize to individuals with relapsing-remitting MS and low physical disability who attend a tertiary care center. Accordingly, study findings may underestimate "true" findings about one's driving performance and may only generalize to a portion of the MS population.

5.1.2 Evaluate Data Collection Procedures and Outcome Measures

The feasibility findings highlight the challenges associated with using driving simulators to assess driving performance. Notably, 25.4% of participants had missing data due to scenario complexity. These findings indicate the importance of scrutinizing kinematic data, often automatically collected by the driving simulator, to examine patterns and understand their implications for driving performance—from study conception to dissemination. In this study, the research student consulted with a research engineer and agreed upon a comprehensive method with five procedures to understand the data: i.e., access, reduction, collection, computation, and verification (see Chapter 2, p. 53-56; Reyes & Lee, 2011, p. 308-323). Nevertheless, missing data still resulted because participants did not drive over the landmark triggers to cue hazardous events to occur. Consultations with simulator industry partners may reduce such challenges and improve data collection procedures and outcome measures for driving simulator studies.

5.1.3 Evaluate the Acceptability and Suitability of the Driving Simulator

Acceptability findings showed that participants' mean responses toward the driving simulator varied from slightly disagree to slightly agree on the Perceived Usefulness and Ease of Use Questionnaire (PUEoU), and from strongly disagree to slightly agree on the System Usability Scale (SUS). These study findings indicate that participants' mean perceptions toward the driving simulator were varied, but, did not include the "strongly agree" scaling responses. This study contributes to the literature by reporting on the acceptability of the simulator for drivers with MS. Whether some responses resulted from fidelity issues, the task difficulty, and/or some participants experiencing symptoms of simulator adaptation syndrome (SAS) is not fully understood. However, considering issues that may have impacted their responses will be a plausible future study to conduct to understand their acceptability (or not) of the driving simulator.

Suitability findings showed that 19% of participants with MS experienced the onset of SAS. These study findings are consistent with the findings reported by (Akinwuntan et al., 2014), which indicate that 14% of participants with relapsing-remitting MS experienced symptoms of SAS. However, the research student also reported additional findings, which showed that the female (vs. male) sex, greater fatigue (Fatigue Severity Scale), reporting more years since last relapse, and reporting taking more medications correlated with increased dizziness while driving the simulator. These findings correspond with at least one of the underlying factors, reported in the literature, that contribute to the occurrence of SAS, i.e., female sex, but not age >70 years or postural/vestibular instability (Akinwuntan et al., 2014; Classen et al., 2011). As MS is more prevalent in women than men, and some individuals may experience vestibular instability, that may be one reason that individuals with MS may be more susceptible to experiencing SAS. Because the occurrence of SAS is under-reported in driving simulator studies for the MS population, understanding the physiological mechanisms will be important for developing and refining mitigation protocols to reduce the onset of SAS during driving assessment or intervention.

5.1.4 Evaluate the Resources and Ability to Manage and Implement the Study

The research student's supervisory and consultative teams consisted of multidisciplinary professionals with expertise in driver rehabilitation science, biostatistics, MS, neurology, occupational therapy, driving simulation, and transportation engineering. Accordingly, the research student had the resources to implement the study, i.e., access to testing and observation rooms, testing equipment, assessment forms, and manuals. However, the navigational driving task of the main driving scenario, which was part of an existing simulator scenario (Alvarez et al., 2019; Alvarez, Classen, Medhizadah, Knott, Asantey, et al., 2018; Alvarez, Classen, Medhizadah, Knott, & He, 2018), did not adequately record participants' strategic driving maneuvers (e.g., addressed recall vs. reasoning, problem-solving). As such, the maneuver will need to be refined (financial investment) for future studies examining high-level reasoning, planning, judging, and problem-solving.

5.1.5 Evaluate Preliminary Clinical and Driving Simulator Test Results

Preliminary test results showed that tactical maneuvers differed between those with MS and without MS. Notably, participants with MS took longer to respond to stimuli in the environment; and more participants with MS rear-ended the vehicle that crossed the lane in front of them. Also, deficits in immediate verbal/auditory recall (CVLT2-IR) and slower divided attention (UFOV2) may indicate driving performance deficits, as both tests moderately correlated with simulated operational, tactical, and strategic maneuvers. Overall, adjustment to stimuli errors may underlie driving performance impairment for drivers with MS. The CVLT2-IR and UFOV2 may be useful for identifying drivers with these driving performance issues.

5.2 Clinical Predictors of Driving Simulator Performance in Drivers with Multiple Sclerosis

Based on the preliminary test results in the feasibility study, the second aim examined if deficits in immediate verbal/auditory recall (CVLT2-IR) and slower divided attention (UFOV2) identified simulated: operational adjustment to stimuli errors in the event when the traffic light changed from green to yellow and then yellow to red; tactical adjustment to stimuli errors in the event when the pedestrian walked out in front of drivers; and/or strategic recall errors in the navigational driving task.

Overall, study findings supported the hypothesis, as deficits in immediate verbal/auditory recall (CVLT2-IR) and slower divided attention (UFOV2) detected tactical errors (i.e., slower maximum response time) in participants with MS. Specifically, drivers with MS took longer to completely stop or pass the pedestrian that walked out in front of them. In addition, drivers with verbal/auditory recall deficits took longer, or did not recall the prior information, to observe road users not following the rules, and as such took longer to respond to the pedestrian. Furthermore, drivers with divided attention deficits took longer to visually search and scan, detect, attend, judge, initiate, and respond to critical roadway information.

These findings indicate that the CVLT2-IR and UFOV2 capture the visual and verbal/auditory recall, processing speed, and divided attention required to respond to the pedestrian. Notably, the pedestrian event requires individuals to attend to multiple visual and auditory stimuli, including the verbal directions provided by the driving simulator to turn right, while concurrently preparing for a lane change, and then responding to the pedestrian who walked in front of them. While drivers mentally process the verbal directions, they begin to initiate a lane change, and then they must respond by either braking or driving around the pedestrian.

Similar to findings in the literature, these findings suggest that impairment in visual processing speed and divided attention may indicate decreased driving performance in individuals with MS (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Classen et al., 2018; Devos et al., 2013; Devos et al., 2017; Harand et al., 2018; Kotterba et al., 2003; Lincoln & Radford, 2008; Morrow et al., 2018; Schultheis et al., 2010). Additionally, these study findings also show that impairment in verbal/auditory recall may indicate driving performance. As such, based on prior and current study findings, immediate verbal/auditory recall and divided attention may be useful clinical indicators of driving performance in drivers with MS.

5.3 Driving Errors that Predict Simulated Rear-End Collisions in Drivers with Multiple Sclerosis

The third aim examined whether simulated adjustment to stimuli errors detected the occurrence of simulated rear-end collisions in drivers with MS vs. drivers without MS. Study findings supported the hypothesis, with shorter time to collision and faster mean speed as sole predictors of simulated rear-end collisions in drivers with MS. Specifically, as compared to control drivers, drivers with MS failed to respond, in an urban environment, to adjusting to environmental stimuli in a timely manner—which resulted in shorter time to collision, faster mean speed, and rear-end collisions in the vehicle crosses lane event. Like on-road studies, these study findings indicate that adjustment to stimuli errors may underlie deficits in driving performance in drivers with MS (Classen et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2017). The findings elucidate the processing speed impairment experienced in individuals with MS. Drivers who experienced a collision did not process the demands posed by the environment at an appropriate pace to avoid a collision. Further, these findings suggest researchers can detect adjustment to stimuli errors via the use of a driving simulator in drivers with MS.

5.4 Contributions to the Literature

Overall, the findings in this dissertation support the notion that deficits in immediate verbal/auditory recall (CVLT2-IR) and slower divided attention (UFOV2) may indicate deficits in driving simulator performance in drivers with MS. The feasibility findings revealed common challenges that occur in driving research for neurologically at-risk populations. Such challenges underscore the need to improve participant recruitment and adherence rates via establishing collaborative multi-site studies that identify and use the same core objective and outcome measures. As driving simulators across sites may differ, there is a need to identify core challenges that may occur, such as simulators with differing fidelity levels (e.g., high fidelity vs. low fidelity) or the simulator related factors, such as refresh rates, that can lead to the onset of SAS. Immediate steps that can be taken to reduce simulator related bias in studies are to: establish collaborative clinician-researcher multi-site studies; and collaborate with simulator industry partners to design and create scenarios and environments that maximize scenarios without jeopardizing comfort.

Multi-site clinician-researcher teams that collaborate within and across jurisdictions may be one strategy that can improve participant recruitment. Notably, such teams can ensure adequate identification of eligible participants while maximizing participant populations. Accordingly, the aim would be to increase the number of participants and generalizability of study findings to the MS population. The feasibility study findings highlight the importance of understanding the perceptions of people with MS towards using a driving simulator as a representation of their driving performance. However, achieving this aim may require a further understanding on participants' perceptions toward acceptability for undergoing a driving simulator assessment. Some strategies that may be considered include designing studies to: Compare responses prior to and after completing a drive on the driving simulator, develop interviews to explore in-depth perceptions, and compare driving performance with individuals' responses via mixed methods.

Clinical tests that measure for visual-cognitive impairment may indicate driving performance deficits in those with MS (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Classen et al., 2018; Devos et al., 2013; Devos et al., 2017; Harand et al., 2018; Kotterba et al., 2003; Lincoln & Radford, 2008; Marcotte et al., 2008; Morrow et al., 2018; Schultheis et al., 2010). In this dissertation, immediate verbal/auditory recall (CVLT2-IR) and divided attention (UFOV2) detected driving performance. Based on these findings, clinician-researcher teams may collaborate to determine and validate clinical tests, such as the CVLT2-IR and UFOV2, that may usefully inform driving performance decisions.

As noted in previous studies, this dissertation found adjustment to stimuli deficits to underlie driving performance impairment in those with MS. Notably, Kotterba et al. (2003) found that drivers with MS made more concentration errors during a monotonous drive that involved responding to infrequent obstacles. Likewise, Devos et al. (2013) and Harand et al. (2018) found that drivers with MS had slower response time, using hand operated buttons, and poorer response accuracy to visual stimuli presented in simulated driving scenarios. In addition to these findings, this dissertation has two additional findings. First, the reaction time and response time in this study are based on foot pedal responses—not hand responses. Hand and foot pedal responses cannot be compared to one another (Society of Automotive Engineers International, 2015). For example, responding through pressing buttons or using turn signal indicators may provide insight into deficits associated with driving skills requiring hand function—but not with the functional driving skill directly related to pedal responses.

Second, most driving simulator studies included a measure of reaction or response time, defined as the time from the start of event to initial reaction or response. In addition to this measure, the research student also measured maximum response time, which indicated the time it took for drivers to visually perceive, initiate, and fully respond (or fail to respond) to stimuli, e.g., brake and come to a complete stop. Through quantifying both measures, study findings provided novel insight to driving performance impairment that may relate to deficits in visual and verbal recall, processing speed, and divided attention. Accordingly, based on these findings, clinician-researcher teams may collaborate to identify and validate core outcome measures, such as pedal responses via measures of reaction time and maximum response time that determine driving performance impairments of drivers with MS.

Establishing collaborations with simulator industry partners may help ensure driving simulator scenarios collect all data required for researchers to confidently and accurately compute and analyze metrics on the driver's performance. One strategy may include having timed vs. landmark triggers to cue events to occur. Through this collaboration, researchers and simulator industry partners may create driving simulator protocols that adequately target the underlying driving performance impairments of drivers with MS. Some scenarios may include having more practice turns in acclimation drives so drivers can appropriately make turns in the main driving scenario. Further, developing and validating mitigation protocols for the MS population may reduce the onset of SAS.

5.5 Limitations

The dissertation's study findings indicate the following biases. First, selection bias may be evident, as all participants voluntarily enrolled in the study. Also, via written informed consent, all participants knew about the neurologist's responsibility to report drivers with conditions that made driving dangerous to the Ministry of Transportation of Ontario. Second, spectrum bias may be evident, as participants with MS over-represented one tertiary MS Clinic (87%), and mostly comprised women (68%) between 30 and 50 years old, with relapsing-remitting MS (vs. progressive MS), and a low to moderate level of physical disability on the EDSS. Furthermore, the age and sex matched participants without MS over-represented one university (86%). Accordingly, study findings may only be generalized to individuals who meet the sample's characteristics for those with MS and without MS.

Preliminary feasibility findings may not have detected significant differences or relationships—as the goal of the study was not to detect statistically significant differences, but to understand feasibility of utilizing clinical tests to indicate driving simulator performance in those with MS. For the clinical predictions, the research student included a sample powered to detect differences between groups. However, the research student recruited 95% of the sample size of drivers with MS. In addition, missing data resulted in quantifying predictions with a sample of 54 and 56 participants, instead of the anticipated 60 participants. As such, calculated results may be an underestimation of the actual results that could have been obtained from a sample of 60.

The research student only examined if visual and cognitive impairment determined through clinical tests contributed to driving performance on a simulator. As such, other demographic, driving behaviour, or SAS characteristics that were not examined may also contribute to participants' driving performance.

Though a driving simulator is a plausible substitute (to on-road driving) for determining driving performance of medically at-risk drivers, it does not measure real-world driving (Shechtman, 2010; Wynne et al., 2019). As such, driving performance on a simulator cannot be used to solely determine someone's fitness to drive. Furthermore, crashes on a driving simulator do not directly relate to crashes in real-world driving (Caffò et al., 2020; Wynne et al., 2019).

The research student used a pre-existing driving simulator scenario that was developed, refined, and validated to identify adjustment to stimuli and visual scanning errors of youth drivers (Alvarez et al., 2019; Alvarez, Classen, Medhizadah, Knott, Asantey, et al., 2018; Alvarez, Classen, Medhizadah, Knott, & He, 2018). Consequently, gap acceptance errors, which also indicate decreased on-road outcomes were not examined (Classen et al., 2017; Classen et al., 2018; Krasniuk et al., 2020; Krasniuk et al., 2017), and the strategic driving maneuver on the driving scenario did not adequately detect the underlying driving performance issues of drivers with MS (e.g., reasoning, problem-solving).

5.6 Strengths

The dissertation contained several strengths. The supervisory and consultative teams consisted of multidisciplinary professionals with expertise in driver rehabilitation science, biostatistics, MS, neurology, occupational therapy, driving simulation, and transportation engineering. Though the study had no external funding, with supervisory, consultative, and community support (e.g., recruitment via MS Clinic, MS Society of Canada), the research student had the resources to implement the study. Inclusion and exclusion criteria ensured that participants had valid graduated drivers' licenses and met the vision standards to legally drive a motor vehicle, thus adhering to the Ministry of Transportation of Ontario standards to drive legally. Though the research student knew participants' diagnoses and clinical test scores, the kinematic data obtained on the driving simulator was objective. Furthermore, video-recording the main scenario and documenting driving outcomes on the standardized assessment form enabled the research student to cross-reference metrics obtained by the driving simulator and those observed from the drive.

This study contributes findings to the feasibility of utilizing visual and cognitive clinical tests that indicated driving simulator performance deficits in drivers with MS. Feasibility findings including reporting on challenges and strategies in the MS driving literature pertaining to recruitment capability, data collection procedures and outcome measures, acceptability and suitability of the driving simulator, resources for implementing the study, and preliminary test results. Findings provided the foundation for determining clinical predictions of driving simulator performance. Further, the research student suggested strategies for improving the feasibility of driving studies for individuals with MS.

Findings for the second aim contribute to the clinical indicators of driving simulator performance during operational, tactical, and strategic driving maneuvers. The study included an adequately powered sample of drivers with MS and a control group of drivers without MS. Further, the study used maximum response time to indicate adjustment to stimuli errors in drivers with MS. Typically, reactions and responses are reported in summary measures of means across trials, which would not provide adequate insight into identifying errors of operational, tactical, or strategic driving maneuvers. As the research student included additional measures to indicate adjustment to stimuli errors, findings elucidated that drivers with MS have difficulty in tactical (vs. operational or strategic) maneuvers.

Findings for the third aim brought novel insights to driving errors that contribute to rear-end collisions on a driving simulator. Notably, failed responses to stimuli, via shorter time to collision and faster mean speed, detect collisions in events that require pedal responses. As adjustment to stimuli errors indicate decreased on-road outcomes, assessing for such errors on a driving simulator may provide useful information about one's driving performance. Driving simulators may be a tool to identify adjustment to stimuli errors because they may not always be present during an on-road assessment. Driving assessors may administer driving simulator assessments prior to taking drivers on the road to anticipate the type of errors drivers may make or to determine on-road readiness.

5.7 Implications

The findings in this dissertation have implications for researchers, policy, and clinical practice.

5.7.1 Research

Drivers with MS who take part in driving studies tend to be 30-to-50-year-old women, with relapsing-remitting MS and low to moderate level of physical disability (Akinwuntan et al., 2018; Akinwuntan, Devos, et al., 2012; Akinwuntan, O'Connor, et al., 2012; Classen et al., 2018; Devos et al., 2017; Krasniuk et al., 2020; Krasniuk et al., 2019; Krasniuk et al., 2017; Lincoln & Radford, 2008; Morrow et al., 2018; Schultheis et al., 2010; Schultheis et al., 2009). Stratifying samples of drivers across age categories, MS diagnoses, or levels of physical disability may shed light on driving performance differences among those factors.

Factors such as the female sex, individuals with a greater level of fatigue, those with more years since their last relapse, and individuals who reported taking more medications, correlated with increased dizziness when exposed to a driving simulator. Though vestibular instability may be prevalent in drivers with MS, the feasibility study findings did not examine whether this factor correlated with the onset of SAS. Furthermore, the factors that contribute to the onset of SAS have not yet been studied in the MS population. Understanding the factors that contribute to SAS is important for developing and improving mitigation strategies for driving simulator assessment and/or intervention for drivers with MS.

The visual-cognitive impairment that cause deficits in driving performance are still not fully understood. Understanding the causal factors that affect driving performance is important for developing targeted intervention protocols to remediate impairments underlying driving performance.

The navigational driving task did not adequately assess simulated strategic driving maneuvers of drivers with MS. Developing and validating strategic driving maneuvers that adequately target driving performance deficits may provide insight to demographic, clinical, and driving characteristics that impact driving performance. To the research student's knowledge, the relative or absolute validity of driving simulator performance on on-road performance of those with MS has not been documented in the English language. Determining the relative or absolute validity of driving simulator outcomes on on-road outcomes may validate decisions about one's driving performance based on a driving simulator assessment.

5.7.2 Policy

The current Canadian fitness to drive standards do not indicate which cognitive abilities if impaired determine fitness to drive. Notably, the standards state that drivers with MS are fit to drive if they meet the conditions to legally drive and have the motor strength, control, and coordination to physically operate a motor vehicle (Canadian Council of Motor Transport Administrators, 2020, p. 160). As impairment in visual processing speed and divided attention predicted driving simulator performance, and are found to be indicators of on-road outcomes in the MS driving literature, clinical tests that measure for such impairment may inform decisions for determining fitness to drive as per the legal Canadian standards.

5.7.3 Clinical Practice

Impairment in visual or auditory processing speed, divided attention, and recall may underlie deficits in driving performance. Physicians, healthcare providers, and licensing board members are encouraged to be cognizant of the visual-cognitive impairment that may impact driving performance. Those who screen for at-risk drivers are encouraged to use clinical tests that measure for such impairment. Further, physicians, other healthcare professionals or other stakeholders who treat and assess patients/clients are encouraged to monitor the deterioration of visual, cognitive, motor abilities that may affect driving performance or fitness to drive.

In this dissertation, deficits in immediate verbal/auditory recall (CVLT2-IR) and divided attention (UFOV2) detected driving simulator performance in drivers with MS. Implementing the CVLT2-IR and UFOV may provide information for understanding the role of episodic immediate verbal/auditory recall, divided attention, and visual processing speed on driving performance. As such, the tests may be used to screen for at-risk drivers and design treatment plans to compensate or remediate for such difficulty. The CVLT2-IR takes about 5 to 10 minutes to complete and costs about $250 USD for the administration manual and test scoring forms. The UFOV takes about 15 minutes to complete and costs about $4100 USD.

Based on findings in this dissertation, tactical adjustment to stimuli errors may underlie driving performance impairment. Nevertheless, driving assessors are encouraged to continue assessing driving performance with scenarios that include operational, tactical, and strategic maneuvers in suburban and urban environments. For a targeted assessment, driving assessors may place greater weight on tactical driving maneuvers that supplement their clinical reasoning for making final decisions about one's driving performance. Tactical driving maneuvers may include foot pedal operations to respond to multiple auditory and visual stimuli in the environment, such as pedestrians walking across the road, cyclists pedaling through intersections, or vehicles cutting across lanes. If driving assessors cannot assess for such maneuvers on a simulator, they may consider assessing them during on-road assessments; and consider documenting such events in their reports about the driver's performance. At-risk drivers identified via driving simulator assessment may be referred to complete a CDE. Since on-road assessments cannot ensure an assessment of hazardous events such as in the driving simulator assessment, using a driving simulator is a plausible substitute to gain useful insight on driving performance.

5.8 Conclusion

This dissertation examined the clinical utility of visual and cognitive tests to indicate driving simulator performance in drivers with MS, when compared with drivers without MS. Through three aims, the dissertation examined: 1) the feasibility of utilizing visual and cognitive clinical tests to indicate driving simulator performance in drivers with MS; 2) if clinical tests contributed to driving performance in drivers with MS; and 3) if simulated adjustment to stimuli errors contributed to understanding simulated rear-end collisions in both groups.

Overall, study findings indicate that utilizing the CVLT2-IR and UFOV2 would be feasible for indicating driving simulator performance in drivers with MS vs. without MS. However, feasibility findings also identified challenges that can occur when conducting studies for drivers with MS. The challenges include low recruitment rates, missing data, and factors that affect the ability to drive a simulator such as the onset of SAS. Study findings supported the second and third aim’s hypotheses. Specifically, deficits in immediate verbal/auditory recall and slower divided attention contribute to slower maximum response time in drivers with MS. Also, adjustment to stimuli errors on a driving simulator predicted simulated rear-end collisions in drivers with MS. Deficits in tactical driving maneuvers may underlie driving performance impairment in those with MS. Physicians, healthcare providers, and licensing board members may screen for driving performance deficits with tests that measure immediate verbal/auditory recall and/or divided attention. Driving assessors may place greater weight on assessing tactical maneuvers, specifically, adjustment to stimuli errors in suburban and urban environments. Examining the clinical indicators of driving performance, using targeted strategic maneuvers, and also considering factors that may affect driving the simulator (i.e., acceptability, SAS), may help understand the impairments of driving performance in drivers with MS.

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Appendices

Appendix A Clinical Tests that Indicate On-Road Outcomes in Drivers with Multiple Sclerosis (*N* = 12 Studies)

Authors (Year)	Clinical Test	On-Road Outcome	Key Findings
Akinwuntan, Devos, et al. (2012)	Barthel Index, Expanded Disability Status Scale, Hospital Anxiety and Depression Scale, Modified Fatigue Impact Scale, Mini-Mental State Exam, Multiple Sclerosis Composite Score, Nine Hole Peg Test, Paced Auditory Serial Addition Test, Rey-Osterrieth Complex Figure, Stroke Driver Screening Assessment, Stroop Colour and Word Test, Trail Making Test, Timed 25-Foot Walk, Useful Field of View™, Visual ability (colour perception, contrast sensitivity, depth perception, glare recovery), and Wechsler Adult Intelligence Scale (Block Design, Digit Symbol)	global rating (pass vs. fail)	23% (10/ 44) failed the on-road assessment. The Stroop Colour test, Stroke Driver Screening Assessment (Road Sign Recognition, Square Matrix Compass, Square Matrix Directions), and central visual processing speed on the Useful Field of View™ (Subtest 1) predicted 91% of pass vs. fail outcomes with 70% sensitivity, 97% specificity, 88% positive predictive value, 92% negative predictive value, 9% misclassified, and 33% error rate.
Akinwuntan, O'Connor, et al. (2012)	Barthel Index, Expanded Disability Status Scale, Mini-Mental State Exam, Paced Auditory Serial Addition Test, Stroke Driver Screening Assessment, and Useful Field of View™	global rating (pass vs. fail)	23% (10/ 44) failed the on-road assessment. The Stroke Driver Screening Assessment predicted 86% of pass vs. fail outcomes with 80% sensitivity, 88% specificity, 67% positive predictive value, 93% negative predictive value, 14% misclassified, and 32% error rate.
Akinwuntan et al. (2018)	Stroke Driver Screening Assessment (Road Sign	global rating (pass vs. fail)	16% (19/ 118) failed the on-road assessment. Drivers who

Authors (Year)	Clinical Test	On-Road Outcome	Key Findings
	Recognition, Square Matrix Compass, Square Matrix Directions), Stroop Colour and Word test, and Useful Field of View™ Subtest 1		failed (vs. passed) had poorer total driving scores on the on-road assessment (failed: total *M* score = 164, *SD* = 12 vs. passed: total *M* score = 190, *SD* = 6, *p* <.0001). The Stroke Driver Screening Assessment (Road Sign Recognition, Square Matrix Compass, Square Matrix Directions), Stroop Colour and Word test, and central visual processing speed on the Useful Field of View™ (Subtest 1) accounted for 27% of the total variance in the total driving score with 82% accuracy, 42% sensitivity, 90% specificity, 44% positive predictive value, 89% negative predictive value, 18% misclassified, and 68% error rate.
Classen et al. (2018)	Expanded Disability Status Scale, Useful Field of View™, and Visual ability (colour perception, contrast sensitivity, depth perception, horizontal peripheral fields, lateral and vertical phorias, visual acuity)	global rating (pass vs. fail), *no.* of adjustment to stimuli, gap acceptance, lane maintenance, signaling, speed regulation, vehicle positioning, visual scanning, and *total* driving errors	17% (5/ 29) failed the on-road assessment. Drivers who failed (vs. passed) made significantly more adjustment to stimuli errors (failed: *M* = 5.2, *SD* vs. passed: *M* = 2.8, *SD* = 2.3, *p* = .02) and gap acceptance errors failed: *M* = .6, .6 vs. passed: *M* = .2, *SD* = .5, *p* = .03). Deficits in far-sighted binocular visual acuity correlated with more adjustment to stimuli errors (r_s = .5, *p* = .006). Slower central visual processing speed on the Useful Field of View™ (Subtest 1) correlated with more gap acceptance errors (r_s = .4, *p* = .03).
Devos et al. (2017)	Assistive device use, Barthel Index, Expanded	*No*. of operational,	102 drivers performed the on-road assessment.

Authors (Year)	Clinical Test	On-Road Outcome	Key Findings
	Disability Status Scale, Hospital Anxiety and Depression Scale, Modified Fatigue Impact Scale, Mini-Mental Status Scale, Nine Hole Peg Test, Paced Auditory Serial Addition Test, Rey-Osterrieth Complex Figure, Symbol Digit Modalities Test-Oral Version, Stroke Driver Screening Assessment, Stroop Colour and Word Test, Trail Making Test, Timed 25-Foot Walk, Useful Field of View™, and Visual ability (colour perception, contrast sensitivity, depth perception, glare recovery, peripheral fields, visual acuity)	tactical, visual-integrative, mixed, and *total* on-road driving scores	Predictors of the: Total operational score: Trail Making Test-B, depth perception, glare recovery, and use of assistive devices. Total tactical score (R^2 = .41): Rey Osterrieth Complex Figure, Stroke Driver Screening Assessment (Square Matrix Directions), Stroop Colour and Word test, mid-distance visual acuity, and vertical peripheral fields. Total visual-integrative score (R^2 = .12): mid-distance visual acuity and vertical peripheral fields. Total mixed score (R^2 = .25): Stroop Colour and Word test and mid-distance visual acuity. Total on-road driving score: Rey Osterrieth Complex Figure, Stroop Colour and Word test, mid-distance visual acuity, vertical peripheral fields, and depth perception.
Krasniuk et al. (2017)	Driving errors: no. adjustment to stimuli errors, no. gap acceptance errors	global rating (pass vs. fail)	22% (8/ 37) failed the on-road assessment. Adjustment to stimuli errors (*OR* = .5, *p* = .006, *95% CI* = [.3, .8]) and gap acceptance errors (*OR* = .05, *p* = .02, *95% CI* = [.0, .7]) predicted pass vs. fail outcomes.
Krasniuk, Classen, Monahan, et al. (2019)	Brief Visuospatial Memory Test-Revised Version, California Verbal Learning Test-Second Edition, Delis-Kaplan Executive Function Sorting Test, Judgement of Line Orientation, Symbol Digit Modalities Test-Oral Version, and	global rating (pass vs. fail)	20% (7/ 35) failed the on-road assessment. As sole predictors, lane maintenance errors (*OR* = .2, *p* = .009, *95% CI* = [.0, .7]) and speed regulation errors (*OR* = .04, *p* = .009, *95% CI* = [.0, .4]) of the strategic driving maneuver predicted pass vs. fail outcomes. Decreased delayed

Authors (Year)	Clinical Test	On-Road Outcome	Key Findings
	Useful Field of View™		visuospatial recall on the Brief Visuospatial Memory Test-Revised Version correlated with more speed regulation errors of the strategic driving maneuver (r_s = -.37, *p* < .05).
Krasniuk et al. (2020)	no. adjustment to stimuli errors and no. gap acceptance errors modeled together	global rating (pass vs. fail)	20% (7/ 35) failed the on-road assessment. Modeled together, adjustment to stimuli errors and gap acceptance errors in suburban environments (*OR* = .4, *p* = .01, *95% CI* = [.2, .8]) or urban environments (*OR* = .3, *p* = .03, *95% CI* = [.1, .9]) predicted pass vs. fail outcomes.
Lincoln and Radford (2008)	Adult Memory and Information Processing Battery, Extended Activity of Daily Living Scale, Paced Auditory Serial Addition Test, Stroke Driver Screening Assessment, Stroop Colour and Word Test, and Test of Motor Impersistence	global rating (pass vs. fail)	38% (13/ 34) failed the on-road assessment. The Stroke Driver Screening Assessment (Road Sign Recognition, Square Matrix Directions) and the Adult Memory and Information Processing Battery (Task B, Design Learning) predicted 88% of pass vs. fail outcomes with 85% sensitivity, 90% specificity, 85% positive predictive value, 90% negative predictive value, 12% misclassified, and 25% error rate [χ^2= (*df* = 6; *N* = 34) = 18.12, *p* = .006].
Morrow et al. (2018)	Brief Visuospatial Memory Test-Revised Version, California Verbal Learning Test-Second Edition, Controlled Oral and Word Association Test, Delis-Kaplan Executive Function System-Sort Test, Employment status, Expanded Disability	global rating (pass vs. fail)	22% (8/ 36) failed the on-road assessment. Unemployment, and impairment on the Immediate Recall Measure of the Brief Visuospatial Memory Test-Revised Version and on the Symbol Digit Modalities Test-Oral Version predicted failing the on-road assessment with 100% sensitivity, 54%

Authors (Year)	Clinical Test	On-Road Outcome	Key Findings
	Status Scale, Judgement of Line Orientation, Paced Auditory Serial Addition Test, and Symbol Digit Modalities Test-Oral Version		specificity, 38% positive predictive value, 100% negative predictive value, 36% misclassified, and 46% error rate [χ^2 (*df* = 1, *N* = 36) = 7.3, *p* = .007].
Schultheis et al. (2009)	Expanded Disability Status Scale (score ≤4.0 vs. score ≥ 4.5)	global rating (pass vs. borderline)	36% (24/ 65) had an Expanded Disability Status Scale score ≥ 4.5. More drivers with scores ≥ 4.5 had borderline outcomes on the on-road assessment [χ^2 = (*df* = 1; *N* = 66) = 25.67, *p* = .001].
Schultheis et al. (2010)	California Verbal Learning Test-Second Edition, Motor-free Visual Perceptual Test-Revised Version, Paced Auditory Serial Addition Test, Symbol Digit Modalities Test-Oral Version, 7/24 Spatial Recall Test, Trail-Making Test-B, Wechsler Adult Intelligence Scale (Vocabulary subtest)	global rating (pass vs. no pass)	19% (12/ 64) did not pass the on-road assessment. The Symbol Digit Modalities Test-Oral Version best predicted pass vs. no pass outcomes (β = .10, *p* = .07). All clinical assessments moderately discriminated 72% of pass vs. no pass outcomes with 84% predictive validity, 25% sensitivity, 98% specificity, 75% positive predictive value, 86% negative predictive value, 15% misclassified, and 77% error rate.

Appendix B Clinical Tests that Indicate Driving Simulator Outcomes in Drivers with Multiple Sclerosis (*N* = 6 Studies)

Authors (Year)	Clinical Test	Driving Simulator Outcome	Key Findings
Devos et al. (2013)	Expanded Disability Status Scale, Functional Reach Test, Hospital Anxiety and Depression Scale, Modified Ashworth Scale, Modified Fatigue Impact Scale, Motricity Index, Paced Auditory Serial Addition Test, Repeatable Battery for the Assessment of Neuropsychological Status, Stroke Driver Screening Assessment, Trail Making Test, Timed 25-Foot Walk, Nine Hole Peg Test, and Visual ability (visual acuity, contrast sensitivity)	Primary driving task: *No.* crashes, *no.* traffic tickets, speed variability (kilometers per hour), *SD* lateral lane positioning (meters), and time to collision (seconds)	No differences in driving performance between 15 drivers with MS vs. 17 without MS. For drivers with MS, the Functional Reach Test (r_s = .6, p <.05), Paced Auditory Serial Addition Test (r_s = .7, p <.01), and Repeatable Battery for the Assessment of Neuropsychological Status (semantic fluency, r_s = .7, p <.01) correlated with speed variability; and Hospital Anxiety and Depression Scale (Depression) correlated with time to collision (r_s = −.8, p <.01).
		Secondary driving task: Response time (seconds) and response accuracy (*no.* correct responses)	Drivers with MS (vs. without MS) had slower response time (*med.* = 3.1 s, *IQR* = 0.8 vs. *med.* = 2.2 s, *IQR* = 0.4, p <.001) and poorer response accuracy (*med.* = 15 correct, *IQR* = 7 vs. *med.* = 24 correct, *IQR* = 3, p <.0001). For drivers with MS, the Hospital Anxiety and Depression Scale (Anxiety) correlated with response accuracy (r_s = −.6, p <.05); Stroke Driver Screening Assessment (Square Matrix Directions) correlated with response time (r_s = .8, p <.01); and Trail Making Test-A correlated with response accuracy (r_s = −.9, p <.0001).

Authors (Year)	Clinical Test	Driving Simulator Outcome	Key Findings
Harand et al. (2018)	Symbol Digit Modalities Test-Oral Version and Test of Attentional Performance (Alertness and Divided attention subtests)	Monotonous highway driving task: *M* lateral lane positioning (kilometers), *SD* lateral lane positioning (kilometers), *M* speed (kilometers per hour), *SD* speed (kilometers per hour), and *no.* of lane crossings	11 drivers with MS (vs. 11 without MS) had higher *SD* lateral lane positioning (p <.05) in the monotonous driving task. No clinical tests correlated with driving performance in drivers with MS.
		Secondary driving task (to monotonous drive): Reaction time (seconds) and sum or errors and omissions	Drivers with MS (vs. without MS) had higher *SD* lateral lane positioning (p <.01), *SD* speed (p <.01), and made more errors and omissions (p <.01) in the divided attention task. For drivers with MS, the Test of Attentional Performance (Divided attention) correlated with driving performance (r = −.9, p <.001).
		Urban driving task: *M* lateral lane positioning (kilometers) and *M* speed (kilometers per hour) at beginning and end of each hazardous event, response time (seconds), and *no.* crashes	No between-group differences in driving performance existed. No clinical tests correlated with driving performance in drivers with MS.
Kotterba et al. (2003)	Expanded Disability Status Scale and Multiple Sclerosis Functional Composite (Nine Hole Peg Test, Paced Auditory Serial Addition Test, Timed 25-Foot Walk)	*No.* crashes and *no.* concentration errors	31 drivers with MS (vs. 10 drivers without MS) drove the same distance on the highway (with MS: *M* = 51.2 km, *SD* = 11.3 vs. without MS: *M* = 53.0 km, *SD* = 8.8), but were involved in more crashes (with MS: *M* = 5, *SD*

Authors (Year)	Clinical Test	Driving Simulator Outcome	Key Findings
			= 4 vs. without MS: *M* = 1, *SD* = 2, p <.001) and made more concentration errors (with MS: *M* = 21, *SD* = 16 vs. without MS: *M* = 7, *SD* = 3, p <.01). For drivers with MS, the Paced Auditory Serial Addition Test correlated with higher crash rates ($r_s = -.3$, p <.05).
Lamargue-Hamel et al. (2015)	Baddeley Double Task, Beck Depression Inventory, California Verbal Learning Test, Expanded Disability Status Scale, Mini-Mental Status Exam, Modified Fatigue Impact Scale, Naming task, Reverse span, Rey-Osterrieth Complex Figure, State-Trait Anxiety Inventory, Stroop Colour and Word Test, Symbol Digit Modalities Test-Oral Version, Test of Attentional Performance, Trail Making Test, and Verbal fluency	*M* lateral lane positioning, *SD* lateral lane positioning, length of road traveled, *M* speed, *SD* speed	52% (16/ 30) of drivers with MS failed the driving simulator task. No clinical tests correlated with driving performance in drivers with MS.
Marcotte et al. (2008)	Cognitive ability (intact vs. impaired), Expanded Disability Status Scale, Grooved Pegboard Test, Hopkins Verbal Learning Test-Revised Version, Paced Auditory Serial Addition Test, Modified Ashworth Scale, Multiple Sclerosis Quality of Life Index, Trail Making Test, and Wechsler Adult Intelligence Scale (Digit Symbol)	Lane tracking task: *M* speed (kilometers per hour), *SD* speed (kilometers per hour), *SD* lateral lane positioning (kilometers), and response accuracy (*no.* that missed at least one target)	17 drivers with MS (vs. 14 without MS) had a higher *M* speed (with MS: *M* = 99.5 km/ h, *SD* = 13.7 vs. without MS: 88.4 km/ h, *SD* = 14.6, p = .03), *SD* speed (with MS: *M* = 5.5 km/ h, *SD* = 2.9 vs. without MS: 2.94 km/ h, *SD* = 1.6, p = .002), and *SD* lateral lane positioning (with MS: *M* = 1.6 km, *SD* = .5 vs. without MS: 1.1 km, *SD* = .3, p = .001). For drivers with MS, cognitive impairment predicted time delay ($R^2_{adj.}$ = .1, p = .09); and spasticity predicted *M* *SD* speed ($R^2_{adj.}$ = .07, p =

Authors (Year)	Clinical Test	Driving Simulator Outcome	Key Findings
			.17).
		Car following task: Coherence (*correlation*), time delay (seconds), and modulus (degrees)	Drivers with MS (vs. without MS) had poorer coherence when following lead vehicle (with MS: M = .6, SD = .2 vs. without MS: .9 km/ h, SD = .1, p <.001). For drivers with MS, spasticity predicted coherence ($R_{2adj.}$ = .2, p <.05) and modulus ($R_{2adj.}$ = .2, p <.05).
Raphail et al. (2020)	Expanded Disability Status Scale, Multiple Sclerosis Functional Composite (Nine Hole Peg Test, Paced Auditory Serial Addition Test, Timed 25-Foot Walk), and Trail Making Test-B	Variability in lateral lane positioning (feet) and speed (miles per hour)	31 participants with MS performed the drive. The Multiple Sclerosis Functional Composite score associated with greater variability in lane position (r = −.5, p = .01).

Appendix C Ethics Approvals from the University of Western Ontario Health Sciences Research Ethics Board and Lawson Health Research Institute

Date: 6 November 2018

To: Dr. Sarah A. Morrow

Project ID: 112525

Study Title: Clinical Predictors of Driving Simulator Performance in Persons with Multiple Sclerosis: A Pilot Study

Application Type: HSREB Initial Application

Review Type: Full Board

Full Board Reporting Date: September 18, 2018

Date Approval Issued: 06/Nov/2018

REB Approval Expiry Date: 06/Nov/2019

Dear Dr. Sarah A. Morrow

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above mentioned study as described in the WREM application form, as of the HSREB Initial Approval Date noted above. This research study is to be conducted by the investigator noted above. All other required institutional approvals must also be obtained prior to the conduct of the study.

Documents Approved:

Document Name	Document Type	Document Date	Document Version
23_October2018_Modified Driver Behavior Questionnaire	Other Data Collection Instruments	23/Oct/2018	
23_October2018_Recruitment Advertisement for drivers with and without MS	Recruitment Materials	23/Oct/2018	
23_October2018_Research Plan	Protocol	23/Oct/2018	
Adapted Motion Sickness Questionnaire	Other Data Collection Instruments	10/Aug/2018	1
Beck Depression Index- Fast Screen	Other Data Collection Instruments	23/Oct/2018	2
BICAMS Administration Instructions	Other Data Collection Instruments	10/Aug/2018	1
Cognitive Assessment - Brief International Cognitive Assessment for Multiple Sclerosis	Other Data Collection Instruments	10/Aug/2018	1
DriveSafety-Phase 2	Other Data Collection Instruments	10/Aug/2018	1
DriveSafetyTM-Phase 1	Other Data Collection Instruments	10/Aug/2018	1
Driving Scenario	Other Data Collection Instruments	10/Aug/2018	1
Driving Simulator Assessment	Other Data Collection Instruments	23/Oct/2018	2
Expanded Disability Status Scale	Other Data Collection Instruments	10/Aug/2018	1
Fatigue Severity Scale	Other Data Collection Instruments	13/Aug/2018	1
LOI and Consent - Volunteers	Written Consent/Assent	23/Oct/2018	
LOI and Consent -Drivers with MS	Written Consent/Assent	23/Oct/2018	
MS Driving Study_Telephone Script	Telephone Script	26/Oct/2018	2

LAWSON FINAL APPROVAL NOTICE

LAWSON APPROVAL NUMBER: R-18-631

PROJECT TITLE: Clinical Predictors of Driving Simulator Performance in Persons with Multiple Sclerosis: A Pilot Study

PRINCIPAL INVESTIGATOR: Dr. Sarah A. Morrow

LAWSON APPROVAL DATE: Tuesday, 13 November 2018

ReDA ID: 4541

Overall Study Status: Active

Please be advised that the above project was reviewed by Lawson Administration and the project:

Please provide your Lawson Approval Number (R#) to the appropriate contact(s) in supporting departments (eg. Lab Services, Diagnostic Imaging, etc.) to inform them that your study is starting. The Lawson Approval Number must be provided each time services are requested.

Dr. David Hill

V.P. Research

Lawson Health Research Institute

Appendix D The Distribution of Continuous Variables

Table 1 summarizes each continuous variable's distribution. Most variables were not normally distributed. The research student examined if variables had outliers through computing *z*-scores (± 3.3; Warner, 2020, p. 101).

Table 1 Distribution of Continuous Variables in Participants with Multiple Sclerosis and Participants without Multiple Sclerosis (*N* = 59)

Continuous variables	Participants	Shapiro-Wilk test		
		value	*df*	*p*
Age (years)	with MS	.9	38	.09
	without MS	.9	21	.81
No. medications	with MS	.9	38	<.0001*
	without MS	.6	21	<.0001*
No. years education	with MS	.9	38	.42
	without MS	.9	21	.88
No. years driving	with MS	.9	38	.09
	without MS	.9	21	.47
No. days driven per week	with MS	.6	38	<.0001*
	without MS	.6	21	<.0001*
No. kilometers driven per day	with MS	.8	38	<.0001*
	without MS	.7	21	<.0001*
Driver Behaviour Questionnaire (*M* score, 1-6)				
Slips	with MS	.9	38	.002*
	without MS	.9	21	.64
Violations	with MS	.9	38	.004*
	without MS	.9	21	.07
Mistakes	with MS	.9	38	.14
	without MS	.9	21	.74
Useful Field of View™ (milliseconds)				
Subtest 1	with MS	.8	38	<.0001*
	without MS	.8	21	<.0001*
Subtest 2	with MS	.3	38	<.0001*
	without MS	.9	21	.03*
Subtest 3	with MS	.6	38	<.0001*
	without MS	.8	21	.001*
Brief International Cognitive Assessment for Multiple Sclerosis				
Symbol Digit Modalities Test-Oral Version	with MS	.9	38	.15
(*no.* correct responses in 90 seconds)	without MS	.9	21	.44
California Verbal Learning Test-Second	with MS	.9	38	.41
Edition (*no.* correct responses out of 80)	without MS	.9	21	.21

Continuous variables	Participants	Shapiro-Wilk test		
		value	*df*	*p*
Brief Visuospatial Memory Test-Revised Version, Immediate Recall Measure (*no.* correct responses out of 36)	with MS	.9	38	.004*
	without MS	.9	21	.06
Brief Visuospatial Memory Test-Revised Version, Delayed Recall Measure (*no.* correct responses out of 12)	with MS	.8	38	<.0001*
	without MS	.8	21	<.0001*
Driving simulator outcomes				
Event 1: Car pulls out in front of driver				
Reaction time (seconds)	with MS	.9	25	.26
	without MS	.9	17	.17
Maximum response time (seconds)	with MS	.9	25	.02*
	without MS	.9	17	.15
Mean speed (meters per second)	with MS	.9	25	.31
	without MS	.9	17	.64
Event 2: Traffic light changes colours				
Reaction time (seconds)	with MS	.8	36	<.0001*
	without MS	.8	21	<.0001*
Maximum response time (seconds)	with MS	.8	36	<.0001*
	without MS	.9	21	.06
Mean speed (meters per second)	with MS	.9	36	.07
	without MS	.9	21	.07
Event 3: Pedestrian walks in front of driver				
Reaction time (seconds)	with MS	.9	36	.41
	without MS	.8	20	.03*
Maximum response time (seconds)	with MS	.9	36	.02*
	without MS	.9	20	.22
Mean speed (meters per second)	with MS	.8	36	<.0001*
	without MS	.8	20	<.0001*
Event 4: Vehicle cuts across lane in front of driver				
Reaction time (seconds)	with MS	.9	34	.44
	without MS	.7	20	<.0001*
Maximum response time (seconds)	with MS	.9	34	.05*
	without MS	.9	20	.32
Mean speed (meters per second)	with MS	.9	34	.36
	without MS	.9	20	.008*

Note. $*p \leq .05$, two-tailed showing non-normal distribution.

Table 2 presents the minimum and maximum *z*-score values of each continuous variable. Six variables had one to two outliers, which consisted of six participants. The research student removed the outliers and reexamined the distribution of each continuous variable.

Table 2 Minimum and Maximum *Z*-Scores Identifying Outliers in Participants with Multiple Sclerosis and Participants without Multiple Sclerosis (*N* = 59)

Continuous Data	Participants with MS		Participants without MS	
	min.	*max.*	*min.*	*max.*
Age (years)	−2.0	1.5	−1.9	1.7
No. medications	−1.2	3.1	−.5	3.1
No. years education	−1.9	2.8	−1.9	2.0
No. years driving	−1.8	1.5	−1.7	1.5
No. days driven per week	−3.4*	.6	−2.2	.6
No. kilometers driven per day	−.9	3.3*	−.8	3.2
Driver Behaviour Questionnaire (*M* score, 1-6)				
Slips	−1.6	3.1	−1.8	1.7
Violations	−1.3	2.9	−1.3	2.2
Mistakes	−1.7	2.4	−1.6	2.3
Useful Field of View™ (milliseconds)				
Subtest 1	−.9	2.8	−.8	2.4
Subtest 2	−.3	5.2*	−1.1	2.3
Subtest 3	−.8	3.7*	−.9	2.9
Brief International Cognitive Assessment for Multiple Sclerosis				
Symbol Digit Modalities Test-Oral Version (no. correct responses in 90 seconds)	−1.9	1.8	−1.5	1.9
California Verbal Learning Test-Second Edition (no. correct responses out of 80)	−2.7	1.7	−1.6	1.7
Brief Visuospatial Memory Test-Revised Version, Immediate Recall Measure (no. correct responses out of 36)	−2.4	1.4	−2.3	1.2
Brief Visuospatial Memory Test-Revised Version, Delayed Recall Measure (no. correct responses out of 12)	−2.4	.9	−2.6	.8
Driving simulator outcomes				
Event 1: Car pulls out in front of driver				
Reaction time (seconds)	−2.6	1.9	−2.6	2.1
Maximum response time (seconds)	−1.6	3.2	−2.2	1.5
Mean speed (meters per second)	−2.8	1.5	−1.9	2.1
Event 2: Traffic light changes colours				
Reaction time (seconds)	−1.2	1.6	−1.1	1.5
Maximum response time (seconds)	−.9	2.4	−1.2	2.2
Mean speed (meters per second)	−1.5	1.9	−1.3	2.4
Event 3: Pedestrian walks in front of driver				
Reaction time (seconds)	−1.8	2.3	−1.4	2.7
Maximum response time (seconds)	−1.7	3.3*	−1.9	1.4
Mean speed (meters per second)	−1.6	2.8	−1.0	3.1
Event 4: Vehicle cuts across lane in front of driver				
Reaction time (seconds)	−2.3	2.3	−1.6	3.6*
Maximum response time (seconds)	−1.5	2.7	−1.5	2.2

Continuous Data	Participants			
	with MS		without MS	
	min.	*max.*	*min.*	*max.*
Mean speed (meters per second)	−2.4	2.5	−1.1	2.2

Note. min. = minimum; max. = maximum
*minimum or maximum *z*-score ± 3.3, identifying an outlier.

Table 3 summarizes each continuous variable's distribution with outliers removed. Most data remained not normally distributed. The research computed non-parametric statistics including all participants to examine the feasibility of utilizing clinical tests to indicate driving simulator performance in participants with MS vs. participants without MS.

Table 3 Distribution of Continuous Variables with Outliers Removed in Participants with and without Multiple Sclerosis (*N* = 53)

Continuous variables	Participants	Shapiro-Wilk test		
		value	*df*	*p*
Age (years)	with MS	.9	33	.14
	without MS	.9	20	.88
No. medications	with MS	.9	33	<.0001*
	without MS	.6	20	<.0001*
No. years education	with MS	.9	33	.54
	without MS	.9	20	.81
No. years driving	with MS	.9	33	.08
	without MS	.9	20	.63
No. days driven per week	with MS	.6	33	<.0001*
	without MS	.6	20	<.0001*
No. kilometers driven per day	with MS	.8	33	<.0001*
	without MS	.7	20	<.0001*
Driver Behaviour Questionnaire (*M* score, 1-6)				
Slips	with MS	.9	33	.006*
	without MS	.9	20	.76
Violations	with MS	.9	33	.001*
	without MS	.9	20	.03*
Mistakes	with MS	.9	33	.30
	without MS	.9	20	.59
Useful Field of View™ (milliseconds)				
Subtest 1	with MS	.8	33	<.0001*
	without MS	.8	20	<.0001*
Subtest 2	with MS	.8	33	<.0001*
	without MS	.9	20	.06
Subtest 3	with MS	.8	33	<.0001*
	without MS	.8	20	.003*
Brief International Cognitive Assessment				

Continuous variables	Participants	Shapiro-Wilk test		
		value	*df*	*p*
for Multiple Sclerosis				
Symbol Digit Modalities Test-Oral Version (no. correct responses in 90 seconds)	with MS	.9	33	.21
	without MS	.9	20	.45
California Verbal Learning Test-Second Edition (no. correct responses out of 80)	with MS	.9	33	.41
	without MS	.9	20	.16
Brief Visuospatial Memory Test-Revised Version, Immediate Recall Measure (no. correct responses out of 36)	with MS	.9	33	.01*
	without MS	.9	20	.11
Brief Visuospatial Memory Test-Revised Version, Delayed Recall Measure (no. correct responses out of 12)	with MS	.8	33	<.0001*
	without MS	.8	20	.001*
Driving simulator outcomes				
Event 1: Car pulls out in front of driver				
Reaction time (seconds)	with MS	.9	23	.27
	without MS	.9	16	.11
Maximum response time (seconds)	with MS	.9	23	.03*
	without MS	.9	16	.25
Mean speed (meters per second)	with MS	.9	23	.27
	without MS	.9	16	.32
Event 2: Traffic light changes colours				
Reaction time (seconds)	with MS	.8	31	<.0001*
	without MS	.8	20	.001*
Maximum response time (seconds)	with MS	.8	31	<.0001*
	without MS	.9	20	.10
Mean speed (meters per second)	with MS	.9	31	.11
	without MS	.9	20	.05*
Event 3: Pedestrian walks in front of driver				
Reaction time (seconds)	with MS	.9	31	.37
	without MS	.9	19	.26
Maximum response time (seconds)	with MS	.9	31	.43
	without MS	.9	19	.18
Mean speed (meters per second)	with MS	.8	31	<.0001*
	without MS	.8	19	.004*
Event 4: Vehicle cuts across lane in front of driver				
Reaction time (seconds)	with MS	.9	30	.49
	without MS	.9	19	.16
Maximum response time (seconds)	with MS	.9	30	.04*
	without MS	.9	19	.23
Mean speed (meters per second)	with MS	.9	30	.31

Continuous variables	Participants	Shapiro-Wilk test		
		value	*df*	*p*
	without MS	.8	19	.006*

Note. *$p \leq .05$, two-tailed showing non-normal distribution.

Appendix E Testing the Assumptions of Multiple Linear Regression

For each predictor variable and dependent variable with continuous data (for models 1 to 5), the research student plotted histograms to examine if variables were normally distributed. The histograms are presented in Figures 1 to 6. As displayed in Figure 2 and Figure 3, participants' scores in divided attention on the Useful Field of View (UFOV2 in milliseconds, see Figure 2) and maximum response time in the traffic light event (in seconds, see Figure 3) were not normally distributed. For the UFOV2, the research student dichotomized scores as those lower than the *mean* vs. the *mean* or higher, i.e., scores <29.7 vs. ≥29.7 milliseconds (Warner, 2020, p. 426-442). For maximum response time in the traffic light event, the research student used participants' response type (stopped vs. failed to stop) and computed a logistic regression model to examine the predictors of the dependent variable.

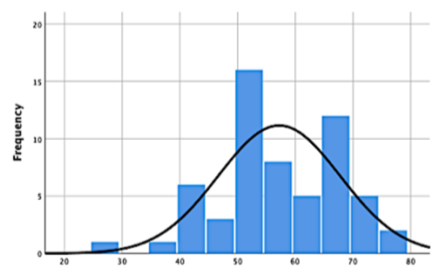

Figure 1. Distribution of Scores on the California Verbal Learning Test-Second Edition Immediate Recall Measure (correct responses out of 80, *N* = 59)

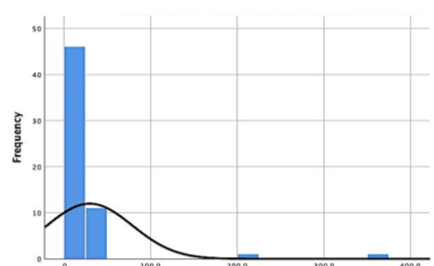

Figure 2. Distribution of Scores on the Useful Field of View Subtest 2 (milliseconds, *N* = 59)

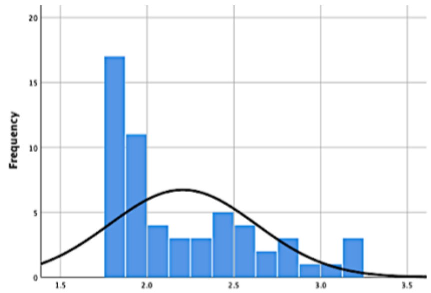

Figure 3. Distribution of Scores for Maximum Response Time in the Traffic Light Event (seconds, *N* = 57)

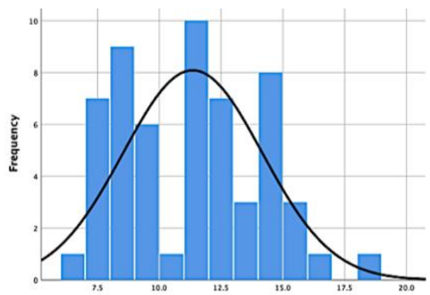

Figure 4. Distribution of Scores for Mean Speed in the Traffic Light Event (meters per second, *N* = 57)

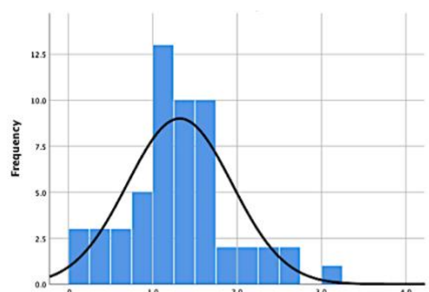

Figure 5. Distribution of Scores for Reaction Time in the Pedestrian Event (seconds, *N* = 56)

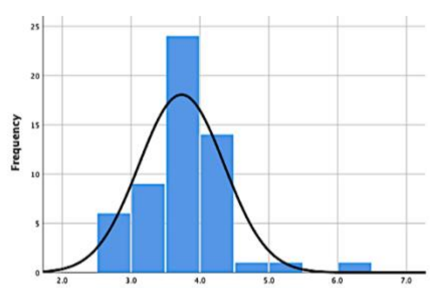

Figure 6. Distribution of Scores for Maximum Response Time in the Pedestrian Event (seconds, *N* = 56)

Next, the research student examined if any variables had multivariate outliers (*z*-score ±3.3, Warner, 2020, p. 101) via plotting residuals of reaction time (see Figure 7) and maximum response time (see Figure 8) in the pedestrian event. As displayed in Figure 8, maximum response time had one outlier (*z* = 3.9, participant score = 6.0 seconds vs. *M* = 3.9 seconds, *SD* = .7), and so the outlier was removed from statistical analyses (Warner, 2020, p. 101). Figure 9 (reaction time) and Figure 10 (maximum response time) display the residual plots with the outlier removed.

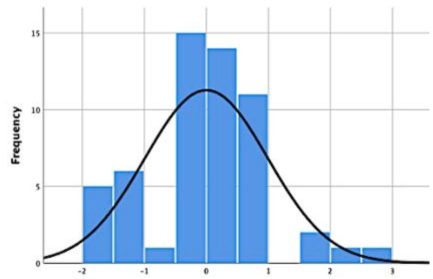

Figure 7. Residual plot of Reaction Time in Pedestrian Event (Seconds, *N* = 56)

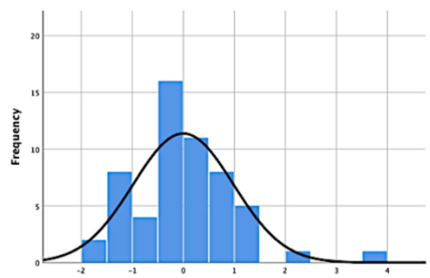

Figure 8. Residual plot of Maximum Response Time in Pedestrian Event (Seconds, *N* = 56)

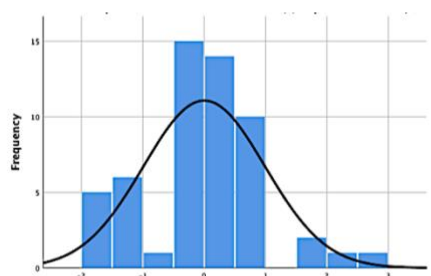

Figure 9. Residual plot of Reaction Time in Pedestrian Event with Outlier Removed (Seconds, *N* = 55)

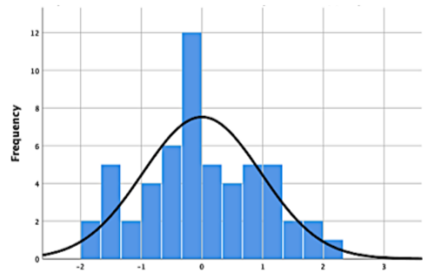

Figure 10. Residual plot of Maximum Response Time in Pedestrian Event with Outlier Removed (Seconds, *N* = 55)

With the outlier removed, the research student examined multivariate linearity of reaction time (Figure 11) and maximum response time (Figure 12) through plotting scatterplots, and homoscedasticity of reaction time (Figure 13) and maximum response time (Figure 14) through plotting multivariate residuals vs. fitted plots.

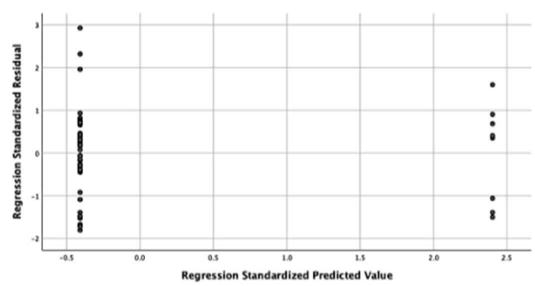

Figure 11. Scatterplot of Reaction Time in Seconds in Pedestrian Event (*N* = 55)

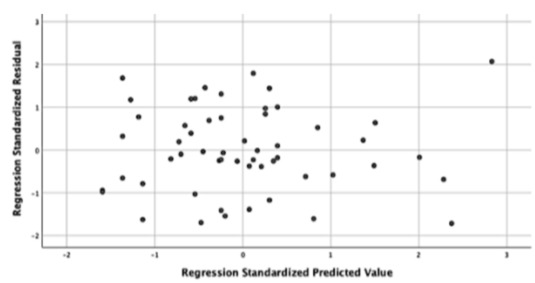

Figure 12. Scatterplot of Maximum Response Time in Seconds in Pedestrian Event (*N* = 55)

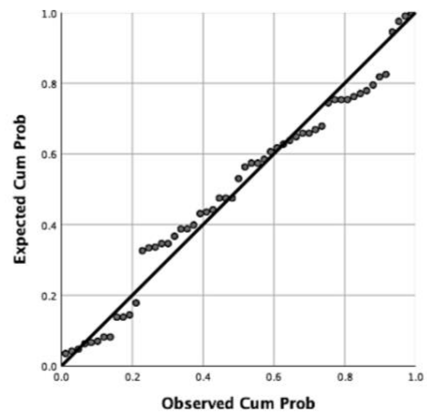

Figure 13. Normal P-P Plot of Standardized Residuals for Reaction Time in Seconds in the Pedestrian Event (*N* = 55)

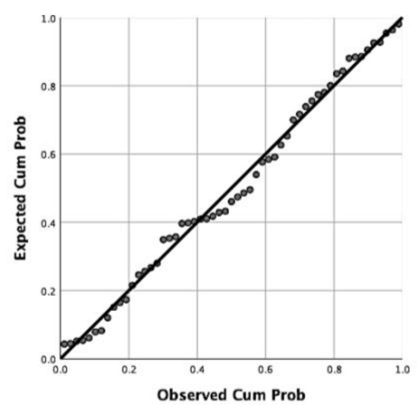

Figure 14. Normal P-P Plot of Standardized Residuals for Maximum Response Time in Seconds in the Pedestrian Event (*N* = 55)

Curriculum Vitae

Sarah Krasniuk MSc, PhD Candidate

Education

1. 2014-Present: Doctor of Philosophy, Health and Rehabilitation Sciences University of Western Ontario, London, ON, Supervisors: Sherrilene Classen PhD, MPH, OTR/L, FAOTA, Sarah A. Morrow MD, FRCPC, MS, Dissertation Topic: Clinical Predictors of Driving Simulator Performance in Drivers with Multiple Sclerosis
2. 2012-2014: Interdisciplinary Certificate in Dementia Studies Lakehead University, Thunder Bay, ON
3. 2009-2012: Master of Science, Kinesiology Lakehead University, Thunder Bay, ON, Supervisor: Jane Taylor PhD, Thesis Topic: Effects of a Virtual Reality Intervention on Postural Adaptation of Children with Movement and Balance Problems
4. 2004-2009: Honours Bachelor of Kinesiology Lakehead University, Thunder Bay, ON Thesis Project: The Effects of the Wii Fit Balance Games on Static and Dynamic Balance of three 9-11-year-old Boys with Developmental Coordination Disorder

Scholarships

1. September 2017-August 2018: Ontario Graduate Scholarship ($15,000 CAD)
2. 2014-2018: Western Graduate Research Scholarship ($20,433.00/year CAD)
3. May-August 2015: Queen Elizabeth II Diamond Jubilee Scholar ($5000 CAD)

Peer-Reviewed Publications

1. Krasniuk, S., Classen, S., Morrow, S. A., Monahan, M., & He, W. Driving Environments that Predict On-Road Outcomes in Persons with Multiple Sclerosis. Transportation Research Part F: Traffic Psychology and Behaviour, 70, 191-198. https://doi.org/10.1016/j.trf.2020.03.003
2. Knott, M., Classen, S., Krasniuk, S., Tippett, M, & Alvarez, L. (2020). Insufficient sleep and fitness to drive in shift workers: A systematic literature review. Accident Analysis and Prevention, 134,105234. doi: 1016/j.aap.2019.07.010.
3. Knott, M., Classen, S., Krasniuk, S., Tippett, M., & Alvarez, L. (2019). Insufficient Sleep and Fitness to Drive in Shift Workers: A Systematic Literature Review Protocol. Injury Prevention, 25, 589-594. doi: 10.1136/injuryprev-2018-042972.
4. Krasniuk, S., Classen, S., Monahan, M., Danter, T., He, W., Rosehart, H., & Morrow, S. A. (2019). A strategic driving maneuver that predicts on-road outcomes in adults with Multiple Sclerosis. Transportation Research Part F: Traffic Psychology and Behaviour, 60, 147-156. doi: https://doi.org/10.1016/j.trf.2018.10.014.

5. Krasniuk, S., Classen, S., Morrow, S. A., Tippett, M., Knott, M., & Akinwuntan, A. (2019). Clinical Determinants of Fitness to Drive in Persons with Multiple Sclerosis: Systematic Review. Archives of Physical Medicine and Rehabilitation, 100(8), 1534-1555. doi:10.1016/j.apmr.2018.12.029.
6. Morrow, S. A., Classen, S., Monahan, M., Danter, T., Taylor, R., Krasniuk, S., Rosehart, H., & He, W. (2017). On-road assessment of fitness to drive in persons with MS with cognitive impairment: A prospective study. Multiple Sclerosis Journal, 24(11), 1499-1506. doi: 10.1177/1352458517723991.
7. Classen, S., Krasniuk, S., Morrow, S. A., Alvarez, L., Monahan, M., Danter, T., & Rosehart, H. (2017). Visual correlates of fitness to drive in adults with Multiple Sclerosis. OTJR: Occupation, Participation and Health, 38, 15-27. doi: 10.1177/1539449217718841.
8. Krasniuk, S., Classen, S., Morrow, S. A., Monahan, M., Danter, T., Rosehart, H., & He, W. (2017). Driving errors that predict on-road outcomes in adults with Multiple Sclerosis. OTJR: Occupation, Participation and Health, 37(3), 115-124. doi: 10.1177/1539449217708554.
9. Classen, S., Krasniuk, S., Alvarez, L., Monahan, M., Morrow, S. A., & Danter, T. (2017). Development and Validity of Western University's On-Road Assessment. OTJR: Occupation, Participation and Health, 37, 14-29. doi: 10.1177/1539449216672859.
10. Classen, S., Krasniuk, S., Knott, M., Alvarez, L., Monahan, M., Morrow, S. A., & Danter, T. (2016). Inter-Rater Reliability of Western University's On-Road Assessment. Canadian Journal of Occupational Therapy, 83(5), 317-325. doi: 10.1177/0008417416663228.
11. Knott, M., Alvarez, L., Krasniuk, S., & Medhizadah, S. (2016). Book review: The reader's brain: How neuroscience can make you a better writer. OTJR: Occupation, Participation and Health 36(2), p. 99. doi: 10.1177/1539449216634080

Peer-Reviewed Presentations

Posters

1. Knott, M., Classen, S., Krasniuk, S., Tippett, M., & Alvarez, L. (2019). Systematic Literature Review of Insufficient Sleep and Fitness to Drive in Shift Workers. Poster for the 2019 Annual American Occupational Therapy Conference, New Orleans, Louisiana, on April 4-7, 2019.
2. Knott, M., Classen, S., Krasniuk, S., Surmacz, M., & Alvarez, L. (2017). Sleepiness and shift worker fitness-to-drive: A systematic literature review. Poster for the Canadian National Driver Rehabilitation Conference, Ottawa, Ontario, on October 12-13, 2017.
3. Knott, M., Classen, S., Krasniuk, S., Surmacz, M., & Alvarez, L. (2017). Sleepiness and shift worker fitness-to-drive: A systematic literature review. Poster for the 2017 Annual Canadian Association of Occupational Therapists Conference, Charlottetown, Prince Edward Island, on June 21-24, 2017.
4. Krasniuk, S., Classen, S., Morrow, S. A., Alvarez, L., Monahan, M., & Danter, T. (2016). The Relationship between visual ability, visual attention, and fitness to drive in adults with Multiple Sclerosis. Poster for the 2016

Faculty of Health Sciences Research Day, London, Ontario, on March 22, 2016.

5. Classen, S., Krasniuk, S., Morrow, S., Monahan, M., Danter, T., & Alvarez, L. (2015). The Relationship between vision, visual attention, and fitness to drive abilities in adults with Multiple Sclerosis. Poster for the Association for Driver Rehabilitation Specialists 2015 Annual Conference, Louisville, Kentucky, on August 1-4, 2015.
6. Classen, S., Krasniuk, S., Morrow, S., Monahan, M., Danter, T., & Alvarez, L. (2015). The Relationship between vision, visual attention, and fitness-to-drive of adults with Multiple Sclerosis. Poster for the 2015 Faculty of Health Sciences Research Day, London, Ontario, on March 25, 2015.

Research Papers and Workshops

1. Krasniuk, S., Classen, S., & Morrow, S. A. (2020). Clinical Determinants of Fitness to Drive in Drivers with Multiple Sclerosis: A Systematic Review. Paper for the Canadian Association of Road Safety Professionals/ La Prévention Routière Internationale 2020 Joint Conference, Montreal, Quebec, June 15-18, 2020. Accepted.
2. Krasniuk, S., Knott, M., Colonna, R., Sultania, R., & Alvarez, L. Driving simulation as an intervention tool: Best available evidence for neurological and psychological disorders. Mini seminar for the Association for Driver Rehabilitation Specialists Annual Conference, Lansing, Michigan, July 25-29, 2020. Accepted.
3. Classen, S., Wolf, T., Reistetter, T., Bundy, A., Schaaf, R., Knott, M., & Krasniuk, S. (2020). Manuscript Writing and Reviewing Academy. Pre-Conference Institute for the 2020 Annual American Occupational Therapy Association Conference, Boston, Massachusetts, March 25, 2020. Accepted.
4. Classen, S., Knott, M., Alvarez, L., Lipowski, J., & Krasniuk, S. (2020). AOTF/OTJR Short course: Advances in Technology to Enhance Manuscript Writing and Publishing. Short course for the 2020 Annual American Occupational Therapy Association Conference, Boston, Massachusetts, March 26-29, 2020. Accepted.
5. Krasniuk, S., Classen, S., & Morrow, S. A. (2020). Driving Environments that Influence On-Road Outcomes of Persons with Multiple Sclerosis. Paper for the 2020 Annual American Occupational Therapy Association Conference, Boston, Massachusetts, on March 26-29, 2020. Accepted.
6. Krasniuk, S., Classen, S., & Morrow, S. A. (2019) A Strategic Driving Maneuver that Predicts On-Road Outcomes in Adults with Multiple Sclerosis. Paper for the 2019 Annual American Occupational Therapy Association Conference, New Orleans, Louisiana, April 4-7, 2019.
7. Classen, S., Page, S., Reistetter, T., Baker, N., Bundy, A., Aldrich, R., Knott, M., Krasniuk, S., & Medhizadah, S. (2019). Manuscript Writing and Reviewing Academy. Pre-Conference Institute for the 2019 Annual American Occupational Therapy Association Conference, New Orleans, Louisiana, April 3, 2019.

8. Krasniuk, S., Knott, M., & Medhizadah, S. (2019). Clinical Implications of Medically At-Risk Drivers. Breakout Session for the 2019 Sandra Edwards Colloquium, Gainesville, Florida, January 26, 2019.
9. Knott, M., Classen, S., Krasniuk, S., Tippett, M., & Alvarez, L. (2018). Systematic Literature Review on Insufficient Sleep and Shift Worker Fitness to Drive: Preliminary Results. Podium Presentation for the 2018 Conference of the Society for the Study of Occupation USA, Lexington, KY, October 11-13, 2018.
10. Classen, S., Alvarez, L., Krasniuk, S., Page, S., Knott, M., & Lipowski, J. (2018). Technology and Manuscript Preparation: A Powerful Must. Short Course for the 2018 Annual American Occupational Therapy Association Conference, Salt Lake City, Utah, April 19-22, 2018.
11. Classen, S., Alvarez, L., Bundy, A., Medhizadah, S., Krasniuk, S., Patomella, A-H., Swanepoel, L., Winter, S., Jeghers, M., & Ried, E. (2018). Fitness to drive and neurological impairments: An evidence-based approach to driving screening, assessment and intervention. In-congress workshop for the 2018 World Federation of Occupational Therapy Congress, Cape Town, South Africa, May 21-25, 2018.
12. Knott, M., Classen, S., Krasniuk, S., Surmacz, M., & Alvarez, L. (2017). Sleepiness and shift worker fitness-to-drive: A systematic literature review. Poster for the 2017 Canadian National Driver Rehabilitation Conference, Ottawa, ON, October 12-13, 2017.
13. Knott, M., Classen, S., Krasniuk, S., Surmacz, M., & Alvarez, L. (2017). Sleepiness and shift worker fitness-to-drive: A systematic literature review. Poster for the 2017 Annual Canadian Association of Occupational Therapists Conference, Charlottetown, PEI, June 21-24, 2017.
14. Classen, S., Alvarez, L., Krasniuk, S., & Medhizadah, S. (2017). Fitness to drive through the lifespan: An evidence-based approach from screening to intervention. Pre-Conference Workshop for the 2017 Association for Driver Rehabilitation Specialists Conference. Albuquerque, New Mexico, July 29, 2017.
15. Morrow, S. A., Krasniuk, S., & Classen, S., & (2017). Platform presentation number 008, Session S24: MS Therapeutics and Clinical Research I on April 25, 2017, at 4:54 PM. Scientific abstract number 2060 entitled "Fitness to drive in persons with MS and cognitive impairment: a pilot study". American Academy of Neurology, 69th Annual Meeting, April 22 to April 28, 2017, Boston, MA.
16. Krasniuk, S., Classen, S., & Morrow, S. A. (2017). Driving errors predicting on-road outcomes in adults with Multiple Sclerosis. Paper for the 2017 Annual Canadian Association of Occupational Therapists Conference, Charlottetown, Prince Edward Island, June 21-24, 2017.
17. Krasniuk, S., Classen, S., & Morrow, S. Relationships between Vision, Visual Attention, and Fitness to Drive in Adults with Multiple Sclerosis. Paper for the 2017 Annual American Occupational Therapy Association Conference & Centennial Celebration, Philadelphia, Pennsylvania, April 1, 2017.

18. Classen, S., Alvarez, L., Krasniuk, S., & Knott, M. (2016). Distraction, drowsiness, and neurological impairment: An evidence-based approach to driving assessment and intervention. Workshop for the 2016 Association for Driver Rehabilitation Specialists Annual Conference, Columbus, Ohio, August 16, 2016.
19. Krasniuk, S., Classen, S., Morrow, S. A., & Alvarez, L. (2016). Vision, visual attention, and fitness to drive in adults with Multiple Sclerosis. Paper for the 2016 Annual Canadian Association of Occupational Therapists Conference, Banff, Alberta, April 22, 2016.
20. Classen, S., Krasniuk, S., Alvarez, L., & Medhizadah, S. (2015). Vision and visual attention as predictors of fitness-to-drive of adults with Multiple Sclerosis. Paper for the 2015 Health and Rehabilitation Sciences Graduate Research Conference, London, Ontario, February 4, 2015.

Invited Presentations

1. Furtado, R., & Krasniuk, S. OT 9541 – An Introduction to the Ethics of Research. Invited Presentation for Western University School of Occupational Therapy on November 29, 2018.
2. Krasniuk, S. Clinical Determinants of Fitness to Drive in Adults with Multiple Sclerosis: A Systematic Literature Review. Invited Presentation for Western University School of Occupational Therapy on April 11, 2017.
3. Krasniuk, S. Growing up with a Silent Disability: A Family's Perspective. Invited Presentation for Western University School of Occupational Therapy on April 7, 2017.
4. Alvarez, L., & Krasniuk, S. Screening and assessment for at-risk drivers across the lifespan. Invited Presentation for Western University School of Occupational Therapy on April 6, 2017.
5. Krasniuk, S., Classen, S., & Morrow, S. Vision, Visual Attention, and Fitness to Drive in Adults with Multiple Sclerosis. Invited Presentation for the Association of Driver Rehabilitation Specialists, Ontario Chapter Meeting, University of Western Ontario, London, Ontario, on May 27-28, 2016.

Graduate Teaching Assistantship

1. 2016-2017: Occupational Therapy 9542, University of Western Ontario, London, ON
2. 2014: Health Policy 3400, University of Western Ontario, London, ON
3. 2009-2011: Kinesiology 4071, Lakehead University, Thunder Bay, ON
4. 2009-2011: Kinesiology 1710, Lakehead University, Thunder Bay, ON
5. 2009-2011: Kinesiology 1711, Lakehead University, Thunder Bay, ON

Intern or Fellowships

1. May 2017-April 2020: Editorial Fellow for OTJR: Occupation, Participation and Health
2. May 2015-August 2015: Intern for "Reducing Road Traffic Accidents in Mwanza, Tanzania" with Western Heads East

Relevant Work Experience

1. 2014: Kinesiologist, Fairway Physiotherapy Clinic, Thunder Bay, ON
2. 2014: Physiotherapist Assistant, Novo Peak Health, Thunder Bay, ON
3. 2012-2014: Physiotherapist Assistant, Centric Health Seniors Wellness, Thunder Bay, ON

Credentials

1. May 29, 2016: CarFit Coordinator and Technician
2. May 28, 2016: NMEDA Training
3. 2014-Present: Registered Kinesiologist (Inactive)
4. 2012-Present: Canadian Society for Exercise Physiology Personal Trainer
5. 2014: Certificate in Jim Bilotta's Soft Tissue Release Program
6. 2012: ABC Dementia Certificate
7. 2012: Nursing Restorative Care and Geriatric Rehabilitation Certificate

Affiliations

1. 2019-Present: Canadian Association of Road Safety Professionals Member
2. 2016-Present: Individual Associate Member of Canadian Association of Occupational Therapists
3. 2016-2018: Member of Association of Driver Rehabilitation Specialists (ADED)
4. 2016-Present: Student Member of Canadian Society of Occupational Scientists
5. 2010-Present: Member of the Ontario Kinesiology Association
6. 2010-Present: Member of the North American Federation of Adapted Physical Activity